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(54) Title: PHARMACEUTICAL PROCESS SYSTEM FOR CREATING AND ANALYZING INFORMATION

(57) Abstract

An interface (10) to a data/information source (20) provides apparatus and methods for entering and accessing data to and from the data/information source. The interface also provides data and information in formats that support data analysis for the three stages of the pharmaceutical process: therapy discovery (12), clinical trial design (14), and pharmacoeconomic analysis (16). The interface utilizes an intuitive graphical user interface for easy input to the interface and manipulation of information received from the data/information source. The analyses data provided by the interface may include, but are not limited to, therapy discovery, clinical trial design, and pharmacoeconomic analysis. These analyses can be used to design treatments, simulate clinical trials, and analyze the patient, carrier and payer benefits of new therapies.

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PHARMACEUTICAL PROCESS SYSTEM FOR CREATING AND ANALYZING INFORMATION

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FIELD OF THE INVENTION

The present invention relates to pharmaceutical information input, analysis, and output. In particular, the invention relates to an interface to a data source. This interface carries out the function of pharmaceutical information input, analysis, and output. The interface could be used with a data source that models biological systems at the cellular or subcellular level, or at the human or patient population level. Alternatively, the interface could be used with a source of collected or archived information or an expert system.

BACKGROUND OF THE INVENTION

New therapy development is extremely speculative. In order to bring a new therapy to market, numerous hurdles must be overcome. Each hurdle involves gaining knowledge about how the therapy works, under what situations it works, and whether or not it is safe. The major hurdles in therapy development are discovering a target therapy, testing it in a human population, and determining whether its effect produces a significant improvement over other therapies for a given disease. Each of these hurdles requires the generation, collection, and analysis of a large amount of data to test hypotheses about the new therapy, i.e., whether or not it is effective; for which patients it is most effective; and whether or not it is an improvement over existing therapies. The automated software system described in this application was developed to help researchers achieve each of these major hurdles.

The pharmaceutical process consists of three identifiable stages: therapy discovery/design, clinical trials, and pharmacoeconomic (PE) assessment. Therapy discovery is the process of finding a leverage point in the biology of the disease process which, if affected, alters the course of disease progression. The pathology of a disease is often so complex that it takes years of research to discover a leverage point that provides a cure or at least relieves the

symptoms. This is clearly one of the most difficult problems facing pharmaceutical research. Current approaches concentrate on standard laboratory experimentation to generate hypotheses and animal tests to further evaluate those hypotheses. This is a very labor-intensive and time-consuming stage in which a positive outcome is not assured. It relies on discovering an insight, which happens in due course rather than on a fixed schedule.

The next stage in the pharmaceutical process involves a formal clinical trial of the target therapy. Clinical trials typically isolate narrowly on a single variable, e.g., the experimental therapy, and use a control group as a baseline from which the variable is measured. Observations from a clinical trial attempt to draw conclusions from statistical differences between the control and experimental groups. Because of the enormous expense of conducting trials large enough to statistically assess a broad range of variables, these observations often fail to take into account the multivariate, dynamic nature of the patients individually or as a group.

Clinical trials are very data intensive and time consuming. The goal is to gather enough evidence to support the desired claims and obtain regulatory approval. A typical cycle for a clinical trial may take several years. For example, designing the trial may take six months, performing the trial may take a year, and analyzing the results may take yet another six months. After years of testing, the results may still be unexpected or difficult to interpret.

The final stage in the pharmaceutical process is analyzing the benefit derived over competing therapies. The pharmaceutical industry is still grappling with how to adequately evaluate the PE benefit of a potential product and there is a dearth of methods for making this assessment. Methods of evaluating relative clinical outcomes and quantifying quality of life differences between competing therapies have not been rigorously formalized. As a result, companies may invest a large amount of money bringing a product to market that cannot achieve an adequate market share to justify the development expense.

A need clearly exists to support, speed and improve the three major stages of the pharmaceutical process. The present invention overcomes prior limitations by supporting the collection, storage, and analysis of the data targeted at each of the major hurdles in the pharmaceutical process. The outcome achieved by the present invention supports the discovery of a target experimental therapy, the design of relevant clinical trials for that therapy, and a comparison of that therapy to existing treatment practices.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide pharmaceutical information input, analysis, and output, in the form of an "interface" to an information source.

It is also an object of the present invention to provide an intuitive user interface to pharmaceutical data and information input, analysis, and output.

It is another object of the present invention to provide apparatus and methods which provide an intuitive software system that guides a user through the process of analyzing data provided by information sources.

It is yet another object of the present invention to provide apparatus and methods to support collection, storage, and analysis of data related to therapy discovery, clinical trial design, and PE analysis.

The above objects are achieved by the present invention, which is a system that supports, speeds, and improves the three major stages of the pharmaceutical development process. Users of the system may reap large financial benefits because the system streamlines the process of searching for a suitable therapy, designing and conducting clinical trials, and evaluating the potential market and consumer benefits of the therapy over current practice.

The dynamic, computer-based system of the present invention receives input, analyzes biological findings and hypotheses, and outputs the results of the analyses. The analyses may be based on data generated by models that provide simulation at the cellular and subcellular levels. The analyses may also be based on other sources of data, such as legacy databases, clinical trials, and expert knowledge. The present invention provides an interface to assist in identifying new therapy targets, develop a better understanding of key biological mechanisms, assess the potential for influencing important clinical outcomes, and evaluate the PE benefit of a proposed treatment.

The present apparatus and methods recognize that these analyses cannot be adequately performed without proper data. Moreover, even if proper data are available, the results still must be analyzed in an appropriate manner to provide information about possible therapy targets, clinical trial designs, and PE variables.

Other objects and advantages of the present invention will become apparent from the following detailed description when viewed in conjunction with the accompanying drawings, which set forth certain embodiments of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows an architecture which may be used to implement the apparatus and methods defined by the present invention;

FIG. 2 is a block diagram showing the Pharmaceutical Process System in accordance with the present invention, including the Pharmaceutical Process Interface;

FIG. 3 is a flow chart showing the sequence of events which advantageously utilizes the disclosed Pharmaceutical Process Interface;

FIG. 4 is a block diagram showing a typical explorer architecture;

FIG. 5 shows a block diagram of the Therapy Discovery Explorer;

FIG. 6 shows a flow chart of processing performed by the Biologic Manipulation Tool;

FIG. 7 shows a sample user interface for the Biologic Manipulation Tool;

FIG. 8 is a flow chart of processing performed by Disease Progression Evaluation Facility;

FIG. 9 shows a sample interface for the Disease Progression Evaluation Facility;

FIG. 10 is a block diagram showing the Clinical Trials Explorer;

FIG. 11 shows a flow chart of the overall processing of the Patient Type Efficacy Module;

FIG. 12 shows an example graphical user interface for the Patient Type Efficacy Module;

FIG. 13 is an example graphical user interface produced by the Patient Results Tool;

FIG. 14 is an example graphical user interface of the Clinical Visualization Tool;

FIG. 15a and FIG. 15b together form a flow chart showing processing performed by the Clinical Trial Design Suite;

FIG. 16 shows an example graphical interface for the Study Design Tool;

FIG. 17 shows an example graphical user interface showing study results from the Study Design Tool;

FIG. 18 is a graphic interface generated by the Trial Analysis Tool showing correlations between patient variables and disease outcomes;

FIG. 19 is a block diagram of the components of the PE Explorer;

FIG. 20a and FIG. 20b together form a flow chart showing how a patient is assigned a categorical designation based on presented symptoms and patient history, and calculation of overall PE benefits for patients, practitioners, and payers;

FIG. 21 provides an example Input/Results user interface for PE analysis of the practitioner generated by the PE Explorer;

FIG. 22 is an example of the PE Explorer user interface showing a summary of the PE analysis for the payer to a user in a report format;

FIG. 23 is a flow chart showing a sequence of analyses designed to determine a categorical designation based on the presented symptoms and patient history in order to then determine what the standard treatment regimen is for the specified patient;

FIG. 24 and FIG. 25 are examples of influence diagrams used to analyze information from the Data/Information Source; and

FIG. 26 is a block diagram showing possible components of the Data/Information Source.

DESCRIPTION OF A PREFERRED EMBODIMENT

A detailed description of a preferred embodiment of the present invention is disclosed herein. It should be understood, however, that the disclosed embodiment is merely exemplary of the invention, which may be embodied in various forms. Therefore, the details disclosed herein are not to be interpreted as limiting, but merely as the basis for teaching one skilled in the art how to make and/or use the invention.

It should be understood that, as used herein, the meaning of the term "interface" is not limited to a mere graphical user interface. Rather, the term, as used herein, is intended to broadly refer to an interface between a user and other computer system components, as well as between components and other applications. Such an interface may include a graphical user interface as well as software and hardware components internal to the system which do not directly interact with the user.

OVERVIEW

The Pharmaceutical Process System, described in detail below, assists a user in overcoming three principle hurdles in the pharmaceutical development process: 1) drug, device, or regimen (hereafter collectively referred to as "therapy") discovery; 2) efficacy analysis, including clinical trial design; and 3) effectiveness analysis, including pharmacoeconomic evaluation. These functions are critical steps in the process of bringing a new therapy to market.

Therapy discovery addresses how to influence the underlying biology of a disease in order to halt or alter its progression. Efficacy analysis answers the question of whether a therapy has an effect on a target disease process. The answer to this question may result in a qualified "yes," in which the product has varied levels of efficacy for different patient groups. Finally, effectiveness analysis compares the proposed experimental treatment to current standard practices for treating the disease to determine if there is any advantage to the new treatment in terms of improved outcome and/or cost. PE evaluation in accordance with the present invention uses expert knowledge to evaluate a proposed treatment and determine outcomes for medical providers, patients, and insurance providers. The Pharmaceutical Process Interface disclosed herein consists of a set of tools that support therapy discovery, efficacy analysis, and effectiveness analysis.

SYSTEM ARCHITECTURE

FIG. 1 shows an exemplary Architecture 80 which may be used to implement the apparatus and methods which make up the Pharmaceutical Process Interface in accordance with the present invention. Common Bus 86 connects Processor 82, Input/Output (I/O) 84, Display 92, RAM 88, ROM 90, Memory 96, and Mass Store 94. Processor 82 may be any type of computer necessary to carry out the computation for the present invention. For example, the computer system could be a Cray supercomputer, a Sun workstation, or an IBM-compatible PC, depending on the applications being used and the complexity of data being analyzed. I/O 84 includes human and system I/O, such as mice or other gesture input devices, modems, and network connections.

When the user interacts with the present invention they can use a typical approach, such as point and click. The present invention may advantageously be designed as an event driven system. A user may direct the system to perform various tasks by selecting items from a menu, clicking on buttons that appear on the screen; or typing in data.

The methodology for displaying data varies widely, depending on the implementation. For example, in Visual Basic, VBX objects can be organized on the screen during software design. The objects then receive and display data during runtime.

ROM 90 may advantageously store an operating system, which may, alternatively, be partially or wholly contained in Processor 82. Memory 96 stores the data which is developed during the course of implementing the present apparatus and methods, and may also store

programs necessary to carry out the invention. The data could also be stored in RAM 88 or Mass Store 94. Display 92 is used to review data entered into the system and data developed by the apparatus and methods described herein. Mass Store 94 may be any memory system, including tape, optical disk, or RAID system for example. The computer system shown is merely exemplary, and is not intended to be limiting. The computer system could be of virtually any size or power, depending on the desired complexity of the Pharmaceutical Process Interface.

The disclosed Pharmaceutical Process Interface apparatus and methods discussed and claimed below are defined by the system architecture that performs the necessary functions to carry out input, analysis, and output of information. The architecture is capable of implementing a wide variety of programs which may be useful in carrying out the invention. While the preferred architecture is disclosed, other architectures could be implemented without departing from the spirit of the present invention.

PHARMACEUTICAL PROCESS SYSTEM

FIG. 2 is a block diagram showing the Pharmaceutical Process System in accordance with the present invention, including Pharmaceutical Process Interface 10. Pharmaceutical Process Interface 10 is comprised of three system components: Therapy Discovery Explorer 12, Clinical Trials Explorer 14, and PE Explorer 16 (each described in detail below). These system components communicate with each other. They exchange pharmaceutical data and other information, as indicated by the bidirectional arrows. The particular implementation of communication between software and hardware components will vary considerably depending on the software and hardware utilized with specific applications of the present invention.

Therapy Discovery Explorer 12 processes data and information from Data/Information Source 20 and Input/Output 18 to support development of a new therapy target which is provided to Clinical Trials Explorer 14 for analysis. Clinical Trials Explorer 14, using the new therapy target developed using Therapy Discovery Explorer 12, develops data to compare the new therapy in different patients under different therapeutic regimens. The new therapy is compared to results achieved through no therapy (placebo) or alternative therapies. The patient and therapy information developed by Therapy Trials Explorer 12 and Clinical Trials Explorer 14 is transferred to PE Explorer 16 which develops further data and assesses differences between an experimental therapy and current standard treatments for a patient. It should be

understood that a person is involved in each step of the process provided by the present invention. The system does not function entirely by itself; that is, decisions regarding a variety of parameters are input by an individual and the system uses the parameters to generate and display data and information to facilitate the decision making process.

It is also contemplated that Explorers 12, 14 and 16 of FIG. 2 could communicate data and information by buffering data or information in either Data/Information Source 20 or Results Database 22. The key point is that each Explorer develops a unique type of data which can in turn be used by a system user or another Explorer. It should also be kept in mind that FIG. 2 is intended to show a broad overview of the Pharmaceutical Process Interface and the specifics of the interface may be varied without departing from the spirit of the present invention.

The components of Pharmaceutical Process Interface 10 communicate with Input/Output 18. Input/Output 18 may include, but is not limited to, video displays, mice, modems, keyboards, light pens, joysticks, communications adapters, etc. Input/Output 18 represents any device capable of exchanging information between a user and Pharmaceutical Process Interface 10. Each of Therapy Discovery Explorer 12, Clinical Trials Explorer 14, and PE Explorer 16 receives information from and sends information to Input/Output 18.

The components of Pharmaceutical Process Interface 10 also communicate with Data/Information Source 20. Data/Information Source 20 (discussed in detail below) stores data and information used by Therapy Discovery Explorer 12, Clinical Trials Explorer 14, and PE Explorer 16, in creating and analyzing pharmaceutical data and information. Data/Information Source 20 stores "original" data and information. "Original" data and information is collected by the user of the system or another outside source. This data may include, but is not limited to, experimental data, standard clinical trial data, simulation results, or other sources of scientific data and/or information.

Finally, the components of Pharmaceutical Process Interface 10 communicate with Results Database 22. Results Database 22 (discussed in detail below), stores "developed" data and information. "Developed" data and information is created by the components of Pharmaceutical Process Interface 10 as the components receive, analyze, and generate data and information. This data and information should be distinguished from data and information which is stored in Data Information Source 20 (discussed below). It should be noted, however, that such intermediate, "developed" data could also be buffered or stored, in whole or in part, by

Data Information Source 20. The data and information developed by Pharmaceutical Process Interface 10 and stored in Results Database 22 is that which the user requested the system to generate.

Pharmaceutical Process Interface 10 may be implemented with a programming language like C, or by using available graphical user interface and application design software packages. For example, Pharmaceutical Process Interface 10 could be implemented using Microsoft Visual Basic® and Microsoft Access®. The principle interactive components of the software are the user interfaces, which display the results of Therapy Discovery Explorer 12, Clinical Trials Explorer 14, and PE Explorer 16, as well as provide a window into Data/Information Source 20 and Results Database 22. These and other features are discussed in detail below.

Pharmaceutical Process Interface 10 is shown for illustrative purposes only as comprising, in a unitary manner, Therapy Discovery Explorer 12, Clinical Trials Explorer 14, and PE Explorer 16. It is also contemplated, however, that each of the components could stand alone, individually occupying the position now occupied by Pharmaceutical Process Interface 10. That is, one Explorer does not necessarily require the other, but certain capabilities are provided by a system in which each of the components shown interacts and exchanges information with other components. For example, a system could be comprised of Data/Information Source 20 containing information typically generated by Therapy Discovery Explorer 12. Such a system could support a stand alone Clinical Trials Explorer 14 which interacts with Input/Output 18, Data/Information Source 20, and Results Database 22.

OVERVIEW OF OPERATION

FIG. 3 is a flow chart showing a possible sequence of events advantageously utilizing the disclosed Pharmaceutical Process Interface 10. Pharmaceutical Process Interface 10 first queries Data/Information Source 20 (30) to produce a profile of a disease progression (32). This profile reflects the average course of disease progression in a given patient population or a given type of patient. Once a profile has been established, a user interacts with the Interface to identify leverage points in the disease biology that alter the course of disease progression.

Pharmaceutical Process Interface 10, via Therapy Discovery Explorer 12, provides a user with methods of altering biological parameters in the disease process. For example, Therapy Discovery Explorer 12 could query Data/Information Source 20 and develop

information showing dynamic changes in the progression of a disease if a certain cytokine (i.e., proteins produced and released by cells that signal other cells) or set of cytokines is blocked. This assists a user in gathering information about combinations of biological changes that might yield a good disease prognosis. An alternative method for designing an appropriate therapy is to start with known therapy effects on human biology. The user would enter the known biological effects of various therapies to see which therapy provides a good disease prognosis. Either alternative helps a user generate hypotheses about potential treatments for a given disease.

Once a therapy or locus of change has been identified by the user with the assistance of Therapy Discovery Explorer 12 (33), Pharmaceutical Process Interface 10 helps the user design an appropriate clinical trial (34) via Clinical Trials Explorer 14. Clinical Trials Explorer 14 uses locus of change information and/or target therapy information to simulate clinical trials to search for patient characteristics that might impact the treatment effect, either weakening or strengthening it. For example, a user might hypothesize that a therapy, while effective in the general population, will have limited effect on patients with diabetes mellitus. Clinical Trials Explorer 14 receives user input regarding a target therapy and particular patient population types, and uses the input to simulate and test a wide variety of patient types by querying Data/Information Source 20 to evaluate the disease outcome for patients receiving the experimental therapy compared to patients receiving a placebo, or alternative therapy, in each relevant patient group (36). Clinical Trials Explorer 14 provides the user with information about ranges of possible treatment effects, including patient groups for which the treatment might have no effect or results in a poor disease outcome.

It should be kept in mind that the data and information in Information/Data Source 20 must reflect the analyses being performed by the components of Pharmaceutical Process Interface 10. Information/Data Source 20 may include a simulation model of biological processes, or other processes related to the analyses performed by the components of Pharmaceutical Process Interface 10. Such a simulation model may receive particular model parameters from the user or system, and run several simulations to derive a disease progression based on different input parameters representing different patient types.

Clinical Trials Explorer 14 then sends the results of the clinical trial simulation(s) to the Results Database or directly to PE Explorer 16 for the next step, PE analysis (38). PE analysis compares a proposed therapy to current standard practice(s) for each patient. For example, based on expert rules collected and implemented as part of PE Explorer 16 code

during development of Pharmaceutical Process Interface 10, PE analysis evaluates the outcome for a particular class of patient, with a particular version of experimental therapy, in terms of cost and quality of life, and yields an evaluation of overall patient satisfaction. PE analysis also evaluates outcomes for the medical practitioner (i.e., the provider) and the insurance carrier (i.e., the payer), using rules supplied by human experts in the disease domain under investigation and implemented in PE Explorer 16 code.

In summary, the preferred embodiment of the Pharmaceutical Process Interface, in accordance with the present invention, consists of three distinct components. Input/Output 18 receives information from a user, Data/Information Source 20 (via the Explorers), and each Explorer; and displays results to the user in the form of graphical information. Data supplied by Information/Data Source 20 may also be analyzed by the three components of Pharmaceutical Process Interface 10. Therapy Discovery Explorer 12 helps the user design a target treatment. Clinical Trials Explorer 14 supports analysis of the results of the treatment across patient groups. Finally, PE Explorer 16 compares the benefits of the treatment to current standard practice. The results of these analyses are stored in Results Database 22. The following sections discuss these components of the invention in detail.

FIG. 4 is a block diagram showing the architecture of a typical explorer. Each Explorer 224 is primarily comprised of Query Processor 226 and Results Synthesizer 228. Each of Query Processor 226 and Results Synthesizer 228 may communicate with one or more adjacent explorers via Communication Path 230. Alternatively, each of Query Processor 226 and Results Synthesizer 228 may communicate with one or more adjacent explorers by selectively buffering data and/or information in Results Database 22.

Query Processor 226 interacts with a user to receive a variety of data and/or information related to an Explorer. Query Processor 226 receives user data/information and translates it into one or more queries. The number and nature of the queries depend on the Sources of data/information in Data/Information Source 20. For example, if Source 1 is a relational database, a relational query would be formed. If Source n is a model, the model would be run with the data/information from the user required to set up the run. If the data/information from the user is not in proper form for directly formulating a query for Data/Information Source 20, Query Processor 226 infers a query to match as closely as possible the needs of the Source being queried. Queries may also include or use information from

another explorer, receiving data/information via 230, and/or retrieving data/information from Results Database 22.

Once Query Processor 226 receives the requested data and/or information from Data/Information Source 20, the data and/or information are sent to Results Synthesizer 228 for further processing. Results Synthesizer 228 is responsible for synthesizing the results from the various Sources into a presentation to the user. Once the user has viewed one or more sets of the synthesized data and/or information from Results Synthesizer 228, the user may request that Results Synthesizer 228 send particular synthesized data and/or information to Data/Information Source 20, Results Database 22, or another explorer for later use. Alternatively, depending on the level of review required by the user, Results Synthesizer 228 may send query results directly to Data/Information Source 20 or Results Database 22 without user review.

THERAPY DISCOVERY EXPLORER

Therapy discovery is the process of finding a method of halting, altering, or preventing a disease process. Therapy Discovery Explorer 12 consists of two tools that support the exploration of changes in the biology of a disease process that have significant effects on the clinical manifestation of the disease. In order to discover a therapy, a researcher evaluates numerous hypotheses about the effect of changes in the underlying disease biology. That is, the researcher evaluates changes in the human biology as a result of the disease. Because of the complexity of the situation, a researcher is normally only able to evaluate a small number of variables. However, Therapy Discovery Explorer 12 enables researchers to readily evaluate extremely multivariate hypotheses and to determine the effect of an intervention on the clinical symptoms displayed by an affected patient.

For example, in infectious diseases, exposure to a pathogen causes the human body to exhibit a variety of defenses. Bolstering these defenses, by either augmenting the immune response or directly killing the pathogen, truncates disease progression. The trick is how to best bolster the defenses in a way that does not damage the patient as a result of amplifying some aspect of the immuno-inflammatory process. Other diseases, such as osteoporosis or diabetes, are not caused by an external agent but by a breakdown in the self-regulatory mechanisms of the body. The key here is to reestablish the mechanisms that regulate body processes. In the case of diabetes, exogenous insulin is often administered to regulate the level of glucose in the blood.

With osteoporosis, exogenous estrogen can be administered to regulate the bone remodeling process and reduce the rate of bone breakdown.

As mentioned above, the pathology of a disease is often so complex that it takes years of research to discover a leverage point that provides a cure or at least relieves symptoms associated with the disease. Therapy Discovery Explorer 12 automates the search for leverage points by providing a multivariable testbed for evaluating hypotheses about how to change the course of a disease.

FIG. 5 shows a block diagram of Therapy Discovery Explorer 12. Therapy Discovery Explorer 12 consists of two components: Biologic Manipulation Tool 220 and Disease Progression Evaluation Facility 222. As shown in FIG. 5, each of Biologic Manipulation Tool 220 and Disease Progression Evaluation Facility 222 communicates with Input/Output 18, Data/Information Source 20 and Results Database 22. Biologic Manipulation Tool 220 allows a user to qualitatively and quantitatively change aspects of biological systems, such as the number of cells available in the immune system or the amount of hormone output by the endocrine system.

For example, a user can change parameters defining the way cells respond by altering or eliminating the production of various cytokines with Biologic Manipulation Tool 220. Alternatively, the user can change a process by eliminating parameters defining the chemical signals that drive the process. Once the user has input the parameter changes into Biologic Manipulation Tool 220, the tool queries Data/Information Source 20 and develops disease progression information based on the user input parameters to see how the changes affect the disease outcome. The results of these analyses are maintained in Results Database 22 for analysis by Disease Progression Evaluation Facility 222. Disease Progression Evaluation Facility 222 assists the user in assessing the effects of biological changes on the course of the disease. It does this by displaying the results in a variety of formats depending on the user's needs.

FIG. 6 shows a flow chart of the processing performed by Biologic Manipulation Tool 220. This tool first presents parameters relating to the biology of interest to the user via a user interface (150). The user interface allows the user to change the input parameters to tailor the type of information developed by Biologic Manipulation Tool 220 (152). The changed and unchanged parameter values are then translated into a query for Data/Information Source 20 (154).

The particular form of the query reflects the type(s) of data and information stored in Data/Information Source 20. In general, the query retrieves data and information about a disease process related to the parameters of interest input by the user. The query is submitted to Data/Information Source 20, and the results of the query are retrieved (155). Upon receiving the data and information from the query, it is determined whether the retrieved results match the original request for data/information from the user (156). If the results do not match, the results are inferred, to the extent necessary, from the retrieved data to match the request as closely as possible (157) (discussed in greater detail below). Finally, Biologic Manipulation Tool 220 passes the query results to Disease Progression Evaluation Facility 222 and/or Results Database 22 (158).

As outlined above, Biologic Manipulation Tool 220 collects the user input parameters related to biologic changes of interest, forms a query from the input parameters, and queries Data/Information Source 20 for the disease outcomes related to those changes. If the precise combination of biologic changes does not exist in this source, Biologic Manipulation Tool 220 retrieves all closely related cases, and infers the outcome associated with the user's parameter selections. Biologic Manipulation Tool 220 makes inferences by using rules, implemented in Biologic Manipulation Tool 220, which are formulated from information supplied by experts in the field. The inferred information/data is formed from rules for aggregating or interpolating across cases, and the results of the analysis are stored in Results Database 22. The process of receiving user input parameters, searching Data/Information Source 20 for information related to the parameters, developing a disease progression profile, presenting the disease progression profile to the user, and storing the disease progression profile may be repeated by the user one or more times. After one or more iterations of developing disease progression in the form of biologic changes and corresponding disease outcomes under a variety of parameters, Results Database 22 contains a series of records of biologic changes and the resulting disease outcomes. This information is then used by Disease Progression Evaluation Facility 222.

It is also contemplated that Biologic Manipulation Tool 220 may infer certain aspects of the user request to properly form a query of Data/Information Source 20. In other words, in Step 154, the user may request certain values or other parameters which may not correspond to directly related data or information stored in Data/Information Source 20. In this case, the query is partially inferred from the user input information to form a query which receives optimal data from Data/Information Source 20.

Fig. 7 shows an example interface to Biologic Manipulation Tool 220. In general, a user interface for this tool reflects the underlying biology being studied. This user interface allows a user to alter parameters used by the Biologic Manipulation Tool 220 in developing data about a disease process. In the example user interface of FIG. 7, a user can manipulate parameters defining levels of cytokine production for various cells, specifically osteoblasts and osteoclasts. Biologic Manipulation Tool 220 uses these parameters by querying Data/Information Source 20 and developing data about osteoporosis. This allows the user to examine how increased or decreased production of cytokines affects the disease process.

The screen shown in FIG. 7 depicts the first two steps of the Biologic Manipulation Tool process (see FIG. 6). The user interface of FIG. 7 displays parameters that can be manipulated by the user. A user is able to enter changes to default values established by the biology of the disease process. After the user makes changes, Biologic Manipulation Tool 220 translates the parameter values into an appropriate query for Data/Information Source 20, queries the source, and retrieves the results of the query.

Biologic Manipulation Tool 220 receives input parameters regarding a biology and/or disease process, accesses Data/Information Source 20 to collect information and data related to the biology/disease parameters, and produces a disease progression profile based on the accessed information. Assume, for example, that the impact of chemical signals on a disease progression is being studied to identify leverage points related to that impact. In such a case, Data/Information Source 20 would store one or more sources of collected information about changes in the course of a disease as a result of altered chemical signals. This data could be the result of an extensive laboratory testing program and/or a computer simulation of the disease. In the latter case, the computer simulation would be run as part of the process of Biologic Manipulation Tool 220 collecting information related to the input parameters.

The second component of Therapy Discovery Explorer 12, Disease Progression Evaluation Facility 222, culls and processes disease progression information generated by Biologic Manipulation Tool 220, and displays to a user relationships between changes in biology and measures of the disease state (i.e., disease parameters). Some changes in the biology may affect one or more disease parameters, but not others. Some changes in the biology may actually worsen the disease progression as measured by the disease parameters. Therapy Discovery Explorer 12 allows a user to repeatedly query Results Database 22 to find the combination of biologic changes that yields the most positive change on all parameters

measuring disease progression. Ultimately, by effectively using Therapy Discovery Explorer 12, the user is able to design or find a therapy that provides the optimal changes in the biology with respect to the effect of the changes on disease outcome.

FIG. 8 is a flow chart showing the processing performed by Disease Progression Evaluation Facility 222. This facility first receives user selections of measures of disease progression to be evaluated (210) and biologic parameter(s) of interest (212). This information is translated into a query for Results Database 22 (214) and retrieved by Disease Progression Evaluation Facility (222). Finally, the results of the query are displayed graphically to the user (218). The graphical display shows how each selected parameter value affects the selected measure of disease progression.

FIG. 9 shows an interface for Disease Progression Evaluation Facility 222. In general, this facility may include a variety of user interfaces, each providing a different view, or method of analysis, of the information developed by the facility. In the example interface of FIG. 9, a user graphically views results of changes in the disease biology on one measure of disease progression as developed by Disease Progression Evaluation Facility 222. In the example interface shown, the graph shows that the changes to TNF (tumor necrosis factor) and IL1 (interleukin 1), input by the user to Biologic Manipulation Tool 220, produce a poor disease outcome as measured by bone loss. This is reflected in the highlighted, high end bone loss values.

An example from osteoporosis illustrates one possible use of the system disclosed herein. Osteoporosis primarily affects postmenopausal women. The cause of osteoporosis can be traced to changes in the bone remodeling process that result from decreased estrogen, decreased mechanical loading on the bone, increased bone remodeling rate due to alteration in certain hormone levels, and a variety of other factors that combine to reduce the density of the bone and increase the likelihood of bone fractures. Treatments of the condition include exogenous estrogen supplements or bisphosphonate therapy.

Bone is a living structure that undergoes constant remodeling throughout the life of an individual. The principle cells involved in bone remodeling are osteoblasts, which build bone, and osteoclasts, which break it down. The action of these two cells is tightly coupled in a normal individual to maintain healthy bone, including optimal remodeling rates and density levels. Any uncoupling of the action of these two cell types can cause suboptimal bone density and weaken the bone. Estrogen is indirectly related to osteoclast activity, such that decreases in

estrogen increase bone breakdown rates, leading to weakened bone. Estrogen supplements reestablish more optimal bone remodeling patterns. However, estrogen supplements have decided drawbacks, including increased risk of breast and uterine cancer.

These insights have emerged through years of studying estrogen supplements. Clearly, a therapy that has the fewest potential side effects is most desirable. Therapy Discovery Explorer 12 can help a user develop information related to such a therapy. Therapy Discovery Explorer 12 accesses Data/Information Source 20, which contains data and information from a clinical trial, laboratory research program, expert judgement, and/or a simulation of bone remodeling. It processes this data and information under instruction of the user. The processing results in a synthesis of the disease progression information from which the user may judge that particular leverage points appear to have the desired or optimum results. This synthesis assists the user in determining whether or not changes in other chemical controls of the bone remodeling process would be effective as possible therapeutic interventions.

For example, assume that Data/Information Source 20 for Therapy Discovery Explorer 12 includes a biological simulation model of bone remodeling. The user inputs parameters to Biologic Manipulation Tool 220 which systematically alters the levels of chemicals used by the model, such as insulin-like growth factor (IGF), interleukin-1 (IL-1), and interleukin-4 (IL-4). These levels could be tuned independently under direction of either user input or Biologic Manipulation Tool 220. The model is then run to establish the results of the changes on the bone remodeling rate and overall bone density. More specifically, the user might input parameters which result in the simulation model causing osteoblasts to produce twice the normal level of IGF and one quarter of the normal levels of IL-1 and IL-4. The simulation is run to project the bone density and remodeling rate that results from these changes, and these projections are saved in Results Database 22. Alternatively or additionally, Data/Information Source 20 may include a database of laboratory research results which are queried to find the results of these changes in laboratory experiments on bone.

Once a series of runs have been executed with different user and system input values and the output results written to Results Database 22, Disease Progression Evaluation Facility 222 enables the user to mine Results Database 22 for relationships between biological changes and disease measures to find the set of changes that produce optimal disease outcomes. In this example, Disease Progression Evaluation Facility 222 repeatedly queries Results Database 22 to find, for example, the range of IGF production (say 95-150% of normal levels) coupled with the

range of IL-1 and IL-4 production (say 50-100% of normal levels) yielding increased bone density levels when estrogen is at post-menopausal levels.

The user, after identifying a biological target, simulates the effect of therapies on the biologic target with Biologic Manipulation Tool 220 to identify a potential experimental therapy. The user does this by inputting the known effect of a therapy on production of IGF, IL-1 and IL-4, and running the simulation until a therapy consisting of one or more therapies is found that maintains these chemicals within their ideal range. Once an experimental therapy is identified, the user can test it across different patient types in Clinical Trials Explorer 14 and evaluate it with respect to current therapeutic practice in Pharmaceutical Process Interface 10.

In summary, Therapy Discovery Explorer 12 assists the user in developing a potential intervention therapy. The potential intervention therapy can be output to Clinical Trials Explorer 14, which can be used to test the potential intervention strategy in one or more simulated clinical trials. The potential intervention strategy can also be analyzed for consumer benefit by PE Explorer 16.

CLINICAL TRIALS EXPLORER

FIG. 10 shows Clinical Trials Explorer 14, which consists primarily of four components. Each of the components of Clinical Trials Explorer 14 interacts with the user (via Input/Output 18), Data/Information Source 20, and Results Database 22, as indicated by the arrows between the elements. The components can be divided into two categories: those that display results for a representative patient (Patient Type Efficacy 160) and those that comprise the clinical trial design suite (Clinical Trial Design 166).

Clinical Trials Explorer 14 provides clinical efficacy analysis. Efficacy analysis performed by Clinical Trials Explorer 14 provides the following exemplary outputs: 1) the impact a treatment may have on a disease process; 2) which patients have the best outcomes; and 3) which patients have the worst outcomes. Other similar questions may also be addressed, while remaining within the spirit of the present invention. These questions are extremely difficult to answer using traditional laboratory/testing practices that are unable to scale up to real world usage conditions. Clinical Trials Explorer 14 provides a testbed for answering these questions in which the user can explore the limits of efficacy under a wide variety of usage conditions. This is a tremendous advantage to the current approach, which often requires multiple clinical trials at great expense to the developer.

As shown in FIG. 10, the primary components of Clinical Trials Explorer 14 are Patient Type Efficacy Module 160 and Clinical Trial Design Module 166. Patient Type Efficacy Module 160 is composed of Patient Results Tool 162 and Clinical Visualization Tool 164. Clinical Trial Design 166 is composed of Study Design Tool 168 and Trial Analysis Tool 170. It should be noted that while FIG. 10 shows only the components of Clinical Trials Explorer 14 interacting with Input/Output 18, Data/Information Source 20 and Results Database 22, the Explorer could also be embodied in a system such as that shown in FIG. 2, without departing from the spirit of the present invention.

FIG. 11 shows a flow chart of the overall processing of Patient Type Efficacy Module (PTEM) 160. This module consists of Patient Results Tool 162 and Clinical Visualization Tool 164. It develops a disease progression for a particular patient type, or class, defined by user input, and displays the disease progression to the user. The user first enters data about patient type into the graphical user interface (240). Patient Type Efficacy Module 160 then translates these entries into a query of Data/Information Source 20 (242), submits the query and retrieves the results (244), and formats the data/information and displays the results to the user (246) in a tabular or chart format. Output would also include the patient characteristics and the precise treatment regimen. Clinical Visualization Component 164 then interprets these results using rules supplied by experts to show how the disease progression might appear clinically to a practitioner. This can be, for example, based on an anatomical representation.

FIG. 12 shows one example of a graphical interface for Patient Type Efficacy Module 160. As shown in FIG. 12, this module allows the user to enter data about a patient. As can also be seen, the labels and selections for describing a patient are intuitive. In general, the labels and selections outline information typical of a patient history, and the figure shows one of many possible examples of such an interface. As can be further seen from FIG. 12, the input information may include, but is not limited to, general information such as Patient Type, Age, Gender, Ethnicity, and Insurance; Disease History; and, Medical Risk Factors.

FIG. 13 is an example of a graphical user interface produced by Patient Results Tool 162. In general, the user interface to this tool shows outcome analysis for a type of patient under study, as shown in the example of FIG. 13. The graphical interface provides a representation of outcomes of a patient under various treatment conditions. The outcome is usually defined to be values for one or more clinical attributes that represent key symptoms of the disease. Results for a patient are displayed, for example, under three typical alternative

treatment regimes: placebo, experimental treatment, and current standard treatment. The example interface of FIG. 13 shows mean bone density outcomes based on a parameter from osteoporosis analysis. The user may select which parameters to view and the time course for changes in the parameters by using the user interface buttons shown at the bottom of the screen in FIG. 13. The parameters and times, however, may be limited by data available from Data/Information Source 20.

FIG. 14 is an example graphical user interface for Clinical Visualization Tool 164. This tool uses the initial condition of the patient acquired from the user's input and data gathered from Data/Information Source 20 to infer likely clinical manifestation of disease progression. The process of inferring the clinical manifestation is based on a set of heuristics (i.e., rules supplied by experts) implemented as part of Clinical Visualization Tool 164. The heuristics should be appropriate for the disease and the parameters that measure the disease progression. For example, as shown in FIG. 14, in an Interface for analysis of osteoporosis the progression of osteoporosis may be displayed as changes in bone density at important loci of the disease: e.g., the vertebra, femur and radius. Shading and/or animation of the anatomical graphical representation of the area being analyzed may be used to show progression of a disease. In FIG. 14, progression is also indicated by percentage bar graphs below each anatomical graphical representation.

FIG. 15a and FIG. 15b together form a flow chart showing the processing performed by Clinical Trial Design 166, and in particular, the processing performed by Study Design Tool 168 and Trial Analysis Tool 170. Study Design Tool 168 and Trial Analysis Tool 170 make up Clinical Trial Design Suite 166. Study Design Tool 168 allows a user to systematically vary patient aspects to analyze the effect of treatment on different types of patients. Trial Analysis Tool 170 supports a user in identifying patient groups in which the therapy has the desired effect and those in which it has a counter intuitive effect.

FIG. 16 shows an example graphical user interface for Study Design Tool 168. The middle portion has several user buttons for assisting in entering requests, data, and information. As shown in FIG. 16, when the user selects the variables for analysis (shown on the left side of the window under "Comparison Variables"), Study Design Tool 168 lists all combinations of those variables (shown by the three blocks on the right side of the window). The user may then elect to run the study for any or all combinations of the variables. That is, Study Design Tool

168 repeatedly queries Data/Information Source 20 to retrieve the results of all combinations of patient types included in the study requested. The new data is stored in Results Database 22.

FIG. 17 shows an example graphical user interface of Study Design Tool 168. This tool gathers and displays results graphically for analysis by the user. The information presented by Study Design Tool 168, as exemplified by FIG. 17, results from queries of Data/Information Source 20 for all variable combinations included in the study. In the example shown, the user elected to evaluate all combinations of estrogen depletion, diabetes status, and smoking status. The results show a bar graph depicting bone loss amount for each factorial combination of those variables.

Trial Analysis Tool 170 provides data visualization and data mining of Results Database 22. As shown in FIG. 18, this tool uses data stored in Results Database 22 to display correlations between patient variables and disease outcomes, allowing the user to better understand and visualize relationships in the data. The user can view correlations in two ways: (1) between patient variables and the treatment outcomes; and (2) between the outcomes and the patient types.

With reference to FIG. 18, the user may select a variety of views of the data. Examples of such choices include, but are not limited to, highlighted disease outcomes associated with combinations of variables under investigation and the disease outcome measures. For example, if the user wishes, the entire range of outcomes stored in Results Database 22 can be shown. The user may then elect to highlight those outcomes that are associated with smokers. This highlights the range of observed disease progression for smokers vs. nonsmokers. The user may condition the highlighting on any number of patient or treatment variables to find combinations that distinguish good and bad disease outcomes.

Trial Analysis Tool 170 provides an extremely helpful graphical methodology for mining Results Database 22 for correlations between patient types and treatment outcomes. For example, the user can explore which combination of patient variables, such as estrogen depletion, smoking history, and diabetes, result in positive outcomes for the experimental treatment of osteoporosis. Perhaps the proposed treatment is very effective in patients with estrogen depletion who do not smoke and do not have diabetes, but is not different from placebo treatments for those patients who smoke. Trial Analysis Tool 170 provides a very effective interface for exploring and depicting these relationships. These patterns can be used directly in the design of a clinical trial.

In summary, Clinical Trials Explorer 14 consists of a set of components for determining how and when a target treatment provides a positive disease outcome. These components combine to store the results of queries for patient types, display and analyze the results for patient types, and evaluate the treatment effects across patient types.

The results of the experimental treatment on different patient types are maintained in Results Database 22 and can be used by PE Explorer 16 in order to compare with current therapeutic practice(s) for the disease within each patient type.

PHARMACOECONOMIC EXPLORER

FIG. 19 is a block diagram of the components of Pharmacoeconomic (PE) Explorer 16. The goal of PE Explorer 16 is to estimate patient, practitioner, and payer (hereafter "constituents") outcomes for the proposed treatment and to compare these outcomes to current standard practice(s). "Outcomes" is intended to mean the comprehensive net result of several factors affecting the particular constituent. To this end, PE Explorer 16 is composed of three modules: Patient Outcome Analysis 100, Practitioner Outcome Analysis 102, and Payer Outcome Analysis 104. To determine outcomes, information in addition to the treatment effect on disease progression must be collected from the user (via Input/Output 18, Results Database 22, or Data/Information Source 20).

Patient outcomes depend on costs to the patient, the quality of life of the patient as a result of the treatment, and the overall treatment effect. Other factors affecting the patient may additionally or alternatively be included. Practitioner outcomes depend on income impact as well as patient satisfaction. Finally, the payer/insurance outcomes depend on cost savings to the company and other factors affecting the payer/insurance.

Each of the three tools, Patient Outcome Analysis 100, Practitioner Outcome Analysis 102, and Payer Outcome Analysis 104, may advantageously be designed as software implementations of weighted influence diagrams. That is, the relationships depicted by connections in an influence diagram (such as those in FIG. 24 and FIG. 25, discussed below) are weighted based on importance, translated into equations, and coded in software.

FIG. 20a and FIG. 20b together form a flow chart of the overall processing performed by PE Explorer 16. In general terms, it accesses information in Data/Information Source 20 based on 1) information generated by another Explorer and stored in Results Database 22, 2) user-selected information generated by another Explorer and stored in Results Database 22, and

3) user input parameters. Calculating outcomes for the different constituents starts with an assessment of the patient's outcome by Patient Outcome Analysis 100.

First, a patient category is assigned (130), and PE Explorer 16 determines what the current standard therapy is for that patient based on the patient's characteristics (132). Data/Information Source 20 and/or the user is queried about patient characteristics. Data/Information Source 20 is then queried on disease outcomes for the patient under current standard practices and the experimental treatment (134). Quality of life differences are then calculated based on disease outcomes for standard practice and experimental treatment (138). The results of the disease outcomes are used to estimate which treatment the patient would require in the future under each therapy (140). In general, better disease outcomes yield reduced future therapy, which leads to reduced costs and increased quality of life.

In addition, relative costs of therapies are compared in terms of both costs accrued during the analysis period and those of the predicted future therapy for the patient (141). Costs to the patient depend not only on market values, but also on the patient's insurance coverage. Once Patient Outcome Analysis 100 has evaluated the patient outcomes, this information is provided to Practitioner Outcome Analysis 102, which determines practitioner outcomes, and to Payer Outcome Analysis 104, which determines payer outcomes (142).

PE Explorer 16 collects data in order to calculate the various outcomes. Each step in the flow chart, until 142, involves collecting or creating data that is used in the calculations in 142. The results are displayed in 144.

Practitioner Outcome Analysis 102 requires user input with respect to a variety of parameters, such as the size and type of practice. For example, large practices benefit by retaining patients (that is, supplying good patient outcomes) while keeping them out of the office for treatment time that could be offered to other patients. Finally, Payer Outcome Analysis 104 determines payer's outcome in terms of whether or not the experimental treatment reduces the costs relative to current standard practice(s). The results of each analysis are provided for display by PE Explorer 16 to the user (144).

PE Explorer 16 performs a clinical effectiveness analysis which answers user questions about whether an experimental treatment compares favorably to existing standard practice(s). While Therapy Discovery Explorer 12 and Clinical Trials Explorer 14 provide great insights to the user into the impact of a therapy on a biology and/or patient population, these insights do not

directly translate into PE comparisons of cost, quality of life, or projections of future treatment. PE Explorer 16 of Pharmaceutical Process Interface 10 addresses these issues directly.

FIG. 21 provides an example if a user input interface for PE Explorer 16 in support of PE analysis of the practitioner. In general, this interface is designed to accept input parameters related to certain types of practices and patients within the practice. As shown in the example interface of FIG. 21, the user enters information about the patient into the interface. This information is used to calculate the outcomes for experimental and standard therapeutic regimens. The content of this screen could alternatively be supplied in whole or in part from Data/Information Source 20. In the example shown, the data/information is supplied entirely by the user.

FIG. 22 provides an example of an Output/Results user interface generated by PE Explorer 16 for PE analysis of the payer. This interface is designed to show PE analysis performed by PE Explorer 16. As shown in the example interface of FIG. 22, outcomes are displayed in a tabular form in which relative evaluations (i.e., the difference in outcomes between experimental and standard therapies) are described textually. Alternatively, actual numerical values of the assessments could be displayed for each PE variable. Finally, the influence diagrams upon which the calculations are based could be displayed and color coded to show the relative outcomes for experimental versus standard therapy.

An example from osteoporosis therapy is illustrative of PE Explorer 16 analysis. In order to determine what the standard treatment regimen is for a patient, the patient is assigned a category designation based on the presenting symptoms and patient history, as shown in FIG. 23. The categorization shown was developed in interviews with experts in the field of osteoporosis disease. It categorizes patients based on their menopausal status, bone loss, and treatment history.

To compare costs of alternative treatment regimens, cost data is obtained by directly coding the costs in the system and/or by querying cost information stored in Data/Information Source 20. The overall cost can then be calculated.

Estimating future therapy requires collecting information and data from experts in the field. This information and data are then used to develop cost analyses which predict future treatment based on a patient's condition. The cost analyses are then performed by PE Explorer 16 under user direction to determine accurate costs.

The standard therapy for each patient category is also based on expert judgment. Experts provide rules about the typical therapeutic practice for a category of patient. FIG. 23 is a decision tree outlining treatments assigned to each of the patient categories. Assignment of standard therapy is based on the patient's classification. This therapy regimen is used in PE Explorer 16 to compare a proposed therapy to the standard treatment that the patient would otherwise receive. It is also used to calculate comparative costs between the proposed regimen and the standard.

The cost of alternative therapies depends on a patient's insurance coverage and the average cost of therapy. A patient's direct cost depends very closely on the patient's insurance. The computation reflects generalities about different types of insurance coverage and average costs of the different types of therapy. The difference between the patient's direct cost for a proposed therapy and the standard therapy is determined by computing the patient's direct cost for each alternative and subtracting. The cost for the proposed therapy may be calculated based on three variables: the treatment regimen, patient's level of compliance, and percentage likely to be covered by the patient's insurance. For example, the therapy used in a particular proposed treatment may cost approximately $1 per day. These costs are added for the number of days of treatment specified by the user. This is multiplied by the patient's level of compliance and then by the percentage not covered by the patient's insurance program to arrive at the patient's direct cost for the proposed therapy.

There are many types of insurance plans, each providing varying degrees of coverage. Types of insurance plans include Indemnity Plans, Managed Care Plans, and Capitated Plans. The following are tables of example cost categorizations for osteoporosis and insurance coverage:

Monitoring or Therapy	Primary Practitioner	Specialist
X-ray monitoring	$200	$400
Sonic monitoring	$80	$150
Hormone replacement	$15/mo	$15/mo
Bisphosphonates	$50/mo	$50/mo

Table 1

Insurance Coverage	
Monitoring:	Indemnity Insurance: Generally not covered unless condition detected - then covered with patient's co-payment rate.
	Managed Care: May be covered as prevention; if not, covered when bone loss detected, at patient's co-payment rate.
Therapy:	Generally, covered under patient's prescription program at co-payment rate.

Table 2

Each of the principle types of insurance coverage, indemnity plans, managed care plans, and capitated plans, dictates how much the patient pays for each type of treatment and how much the insurer pays. The other principle component of the cost analysis is the average cost for a treatment depending on the type of practice and the area of the country in which the treatment is provided. For example, in the osteoporosis example, treatment costs depend on whether the practitioner is a primary practitioner or a specialist, which in turn may depend on the severity of the patient's condition as well as the type of insurance the patient has.

PE analysis performed by Patient Outcome Analysis 100 addresses the patient's quality of life, including which therapy is likely to provide the fewest side effects, least time and effort on the part of the patient, and the best overall outcome. Each of these factors is modified by patient variables. For example, patients who have nonexempt employment status are more likely to be concerned about time away from their job. These factors combine to yield a quality of life comparison between the therapies.

One variable that strongly affects both patient outcome and quality of life is the extent of further treatment necessary to contain disease progression following the time period under analysis. Returning to the patient categories, patients who have an outcome that moves them between categories are likely to encounter the level of treatment needed by members of that new category in the future. Thus, if the condition can be contained, so will future therapy and costs.

As mentioned above, step 142 of FIG. 20b calculates the overall PE benefits for patients, practitioners, and payers (i.e., insurers). For example, the analysis may develop patient costs by calculating variables associated with compliance, the level of insurance coverage, and the costs of treatment. Insurance costs use similar types of insurance- related data. FIG. 24 and

FIG. 25 are examples of influence diagrams used in analyzing information from Data/Information Source 20. The particulars of FIG. 24 and FIG. 25 are from osteoporosis analysis. To yield overall patient satisfaction, patient outcomes are based on a weighted combination of the cost analysis and quality of life variables. Calculating practitioner outcomes depends on patient satisfaction, practice volume, and primary insurance coverage of patients in the practice. Finally, payer outcomes depend on the cost of the therapy and the projected future therapy. The general rule is that averted or delayed costs benefit the payer.

As mentioned above, FIG. 22 is an example of PE Explorer 16 showing a summary of the analysis to a user in a report format. The results can additionally or alternatively be displayed as a graphical representation of the influence diagrams that guide the analyses and the associated levels for each of the PE variables. In this manner, the user is able to see graduated differences between the treatment regimens in addition to a final summary of the analysis.

In summary, PE Explorer 16 collects input variables for the patient to be analyzed and analyzes the information obtained from Data/Information Source 20 in order to evaluate the clinical effectiveness of the experimental treatment for a given patient. The Explorer also analyzes the PE outcome of the experimental treatment for the practitioner and payer.

DATA/INFORMATION SOURCE

FIG. 26 is a block diagram showing possible components of Data/Information Source 20. Data/Information Source 20 is accessible via user-friendly graphical user interfaces provided by the Explorers, as discussed above, for data entry, query, and reporting. Implementation of such graphical user interfaces are well-known in the art, and will not be discussed in detail here.

The particular method of querying Data/Information Source 20 used by each Explorer depends on the format of the data or information. For example, if Data/Information Source 20 included an SQL database, submitting a query to the SQL database would require constructing the query using correct SQL syntax. If Data/Information Source 20 included an expert system implemented in a rule-based tool, such as CLIPS or PROLOG, the Explorer would launch and exchange information with the expert system. If Data/Information Source 20 also included a simulation model, the system would launch the simulation code/tool of the model and send the simulation model appropriate information. Information flow in Pharmaceutical Process Interface 10 can occur dynamically through a facility like DLL, VBX, OCX under Microsoft

Windows, or through files written on a hard disk that are accessible to system software components, or through a shared database such as Results Database 22. It should be understood that, in each of the three examples discussed above, the Explorer and Data/Information Source 20 exchange information in some way.

Pharmaceutical Process Interface 10 organizes data/information provided to and received from objects that appear on the screen so that the other components of the system using the information can interpret the data/information correctly. The structures used to ensure this vary widely depending upon the particular implementation. Factors which may affect this include the sources of available data and the software language/tool used for implementation. For example, data/information may be temporarily stored in arrays, lists, streams, or custom structures defined in the implementation.

As shown in FIG. 26, Data/Information Source 20 may include, but is not limited to, Clinical Trials Data 180, Experimental Data 181, Expert Knowledge 182, Case-Based Data 184, and/or Simulation Model(s) 186. Each of these may be used by one or more of the Explorers shown in FIG. 2 and described above.

It should also be kept mind that Therapy Discovery Explorer 12, Clinical Trials Explorer 14, and PE Explorer 16, can exchange information directly with each other.

Examples of sources for Data/Information Source 20 include, but are not limited to, expert knowledge bases, historical databases, clinical trials results, and/or computer models. A single Data/Information Source 20 may contain multiple types of information therein.

The availability of the right data is crucial to generating informed analyses. Pharmaceutical Process Interface 10 is connected to Data/Information Source 20, which stores data collected independently of Pharmaceutical Process Interface 10.

Clinical Trials Data 180 may include, for example, disease outcomes for all patients in a clinical trial and reflects the formal methodology used in that trial. Laboratory results include data collected in a research program on the target disease.

Experimental Data 181 may include, for example, results obtained from using animal models, or other similar types of studies.

Expert Knowledge 182 could be, for example, in the form of an expert system or knowledge base. Expert opinion needs to be rigorously collected and formalized for use with the system.

Case-Based Data 184 may include, for example, historical information about individual instances collected in a relatively informal manner over time, perhaps years. This data would most likely be collected about patients from private practices. On the other hand, it could be formally collected in long-term longitudinal studies.

Finally, Simulation Model 186 of the disease process could supply the necessary data based on a simulation of the disease effects over time. The level of detail in the disease model could vary depending on the needs.

What is more important, however, is not the form of the data but the content. In order to be useful in the analyses conducted by the Explorers described herein, certain content must be available in Data/Information Source 20 regardless of its form.

For example, this source must be able to supply detailed biological-level information to Therapy Discovery Explorer 12. In order to evaluate a hypothesis about, for example, the relationship of IL-4 to osteoporosis, Data/Information Source 20 must supply information about how changes in IL-4 affect bone density. The best sources of this information would be a laboratory research program, expert opinion, or a computer model.

Clinical Trials Explorer 14 requires information about patient types and their relation to disease outcomes. This explorer can directly use information about how an experimental treatment affects disease outcomes (i.e., information that might stem from an actual clinical trial, historical data, or a disease simulation). Alternatively, Clinical Trials Explorer 14 could infer disease outcomes based on expertise in the field relating to the disease codified in an expert system.

PE Explorer 16 requires not only data concerning outcomes from the experimental treatment needed by Clinical Trials Explorer 14, but also data concerning the effects of standard therapeutic practices on disease outcomes. This additional information can be supplied by a historical record, expert opinion, and/or a computer model of the disease.

Each of the Explorers must be able to access information from Data/Information Source 20. Thus, in addition to having the necessary content, the format of the data must be sufficiently specified to implement the software which accesses it. If, for example, the data is stored in an SQL database, the software implementation would include code to construct the SQL queries necessary to retrieve the relevant information.

It should be further noted that part of the process of creating Pharmaceutical Process Interface 10 may include creating Data/Information Source 20. If the necessary data are

available, it may be as simple as entering it into a database or interfacing to an existing database. Alternatively, development of Data/Information Source 20 may involve the relatively complex process of constructing a knowledge base or building a disease simulation. The design and construction of the Explorers are directly linked to the design and construction of Data/Information Source 20, which may need to be created prior to building the Explorers.

RESULTS DATABASE

The components of Pharmaceutical Process Interface 10 are also connected to Results Database 22. This database stores the final analyses of Therapy Discovery Explorer 12, Clinical Trials Explorer 14, and PE Explorer 16 for subsequent viewing and further manipulation by the system or user. It should be kept in mind that some of the information generated by the components of Pharmaceutical Process Interface 10, including final analyses information, may also be transferred to other components, Input/Output 18, and/or Data/Information Source 20.

The above descriptions of preferred embodiments have been given by way of illustration only and numerous other embodiments of the subject invention may become apparent to those skilled in the art upon consideration of the above description and the attached drawings. Accordingly, limitations on the scope of the subject invention are to be found only in the claims set forth below.

CLAIMS

We Claim:

1. An apparatus for therapy data analysis and creation comprising:

a data/information source for storing information related to therapy data analysis and creation; and

a process interface for accessing the data/information source and for analyzing and creating therapy data, the process interface including, a therapy discovery explorer for receiving one or more biologic parameters and developing information relating biology change to disease change.

2. The apparatus according to claim 1, wherein the therapy discovery explorer comprises a biologic manipulation tool for producing one or more profiles of disease progression based on the one or more biologic parameters.

3. The apparatus according to claim 2, wherein the biologic manipulation tool queries the data/information source based on the one or more biologic parameters to produce the one or more profiles of disease progression.

4. The apparatus according to claim 2, wherein the biologic manipulation tool comprises a graphical user interface for entering the biologic parameters.

5. The apparatus according to claim 1, wherein the therapy discovery explorer further comprises a disease progression evaluation facility for analyzing disease progression based at least in part on information retrieved by the biologic manipulation tool from the data/information source and for developing information relating biology change and disease change.

6. The apparatus according to claim 1, wherein the therapy discovery explorer comprises a disease progression evaluation facility for analyzing one or more profiles of disease progression

and developing the information relating biology change and disease change based on the profiles.

7. The apparatus according to claim 6, wherein the disease progression evaluation facility comprises target treatment development support for identifying at least one therapy.

8. The apparatus according to claim 6, wherein the disease progression evaluation facility comprises a user interface element for creating a display of the information relating biology change and disease change.

9. An apparatus for therapy data analysis and creation comprising:

a data/information source for storing information related to therapy data analysis and creation; and

a process interface for accessing the data/information source and for analyzing and creating therapy data, the process interface including, a clinical trials explorer for developing disease progression information based on patient type information and treatment information.

10. The apparatus according to claim 9, wherein the clinical trials explorer includes: a patient type efficacy module for receiving patient type information and developing disease progression information based on the patient type information.

11. The apparatus according to claim 9, wherein the clinical trials explorer comprises a visualization component for displaying patient type disease progression information from rules-based analysis.

12. The apparatus according to claim 9, wherein the clinical trials explorer includes, a clinical trial design suite for determining one or more disease outcomes for one or more patient types over a specified period of time with respect to at least one therapy.

13. The apparatus according to claim 12, wherein the clinical trial design suite comprises a study design tool for developing information relating patient types and disease progression based on analysis variables.

14. The apparatus according to claim 12, wherein the clinical trial design suite comprises a trial analysis tool for developing correlations between patient variables and disease outcomes.

15. An apparatus for therapy data analysis and creation comprising:

a data/information source for storing information related to therapy data analysis and creation; and

a process interface for accessing the data/information source and for analyzing and creating therapy data, wherein the process interface includes a graphical representation of relevant anatomy that modifies to show disease progression.

16. An apparatus for therapy data analysis and creation comprising:

a data/information source for storing information related to therapy data analysis and creation; and

a process interface for accessing the data/information source and for analyzing and creating therapy data, the process interface including, a pharmacoeconomic explorer for performing effectiveness analysis on therapy data.

17. The apparatus according to claim 16, wherein the pharmacoeconomic explorer includes at least one outcome analyzer for comparing a proposed therapy to current standard therapy for a particular constituent.

18. The apparatus according to claim 17, wherein the pharmacoeconomic explorer receives information characterizing clinical trial results to support the outcome analyzer.

19. The apparatus according to claim 16, wherein the pharmacoeconomic explorer includes, at least one outcome analyzer for developing information relating a therapy to a particular constituent outcome.

20. The apparatus according to claim 19, wherein the pharmacoeconomic explorer receives information characterizing clinical trial results to support the outcome analyzer.

21. An apparatus for therapy data analysis and creation comprising:

a data/information source for storing at least two sources of data and information related to therapy data analysis and creation;

a process interface for accessing at least two sources from the data/information source and for analyzing and creating therapy data; and

a results database for storing intermediate and final results of the created and analyzed data.

22. A system for biological data analysis used in developing, testing and evaluating therapies, comprising:

at least two distinct data/information sources providing biological information;

at least one interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of a desired biological system;

wherein the appraised data is applied to develop, test and evaluate therapies relating to the desired biological system.

23. The system according to claim 22, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

24. The system according to claim 22, wherein the at least one interface is chosen from the group consisting of a therapy explorer interface, a clinical trials explorer interface, and a pharmacoeconomic explorer interface.

25. The system according to claim 24, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

26. The system according to claim 22, wherein the system includes a therapy explorer interface, a clinical trials explorer interface, and a pharmacoeconomic explorer interface.

27. The system according to claim 26, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

28. The system according to claim 22, wherein results produced by the at least one interface are a distinct data/information source which may be used by a second interface in providing reliably appraised data of a desired biological system.

29. The system according to claim 28, wherein the at least one interface is chosen from the group consisting of a therapy explorer interface, a clinical trials explorer interface, and a pharmacoeconomic explorer interface.

30. The system according to claim 29, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

31. The system according to claim 28, wherein the system includes a therapy explorer interface, a clinical trials explorer interface, and a pharmacoeconomic explorer interface.

32. A system for biological data analysis used in developing, testing and evaluating therapies, comprising:

at least two distinct data/information sources providing biological information;

a therapy explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the underlying biology of a disease;

wherein the appraised data is applied to develop, test and evaluate therapies relating to the desired biological system.

33. The system according to claim 32, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

34. The system according to claim 32, wherein the system also includes a clinical trials explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the efficacy of specific therapies for a disease.

35. The system according to claim 34, wherein the system also includes a pharmacoeconomic explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the effectiveness of a proposed disease treatment when compared to standard therapies.

36. The system according to claim 35, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

37. The system according to claim 32, wherein the system also includes a pharmacoeconomic explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the effectiveness of a disease treatment when compared to standard therapies.

38. The system according to claim 37, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

39. The system according to claim 32, wherein results produced by the therapy explorer interface are a distinct data/information source which may be used by a second interface in providing reliably appraised data of a desired biological system.

40. The system according to claim 39, wherein the system also includes a clinical trials explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the efficacy of specific therapies for a disease.

41. The system according to claim 40, wherein the system also includes a pharmacoeconomic explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the effectiveness of a disease treatment when compared to standard therapies.

42. The system according to claim 41, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

43. The system according to claim 39, wherein the system also includes a pharmacoeconomic explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the effectiveness of a disease treatment when compared to standard therapies.

44. The system according to claim 43, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

45. A system for biological data analysis used in developing, testing and evaluating of therapies, comprising:

at least two distinct data/information sources providing biological information;

a clinical trials explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the efficacy of specific therapies for a disease;

wherein the appraised data is applied to develop, test and evaluate therapies relating to the desired biological system.

46. The system according to claim 45, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

47. The system according to claim 45, wherein the system also includes a pharmacoeconomic explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the effectiveness of a disease treatment when compared to standard therapies.

48. The system according to claim 47, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

49. The system according to claim 47, wherein results produced by the clinical trials explorer interface are a distinct data/information source which may be used by a second interface in providing reliably appraised data of a desired biological system.

50. The system according to claim 49, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

51. A system for biological data analysis used in developing, testing and evaluating therapies, comprising:

at least two distinct data/information sources providing biological information;

a pharmacoeconomic explorer interface integrating data received from the at least two distinct data/information sources to provide reliably appraised data of the effectiveness of a disease treatment when compared to standard therapies;

wherein the appraised data is applied to develop, test and evaluate therapies relating to the desired biological system.

52. The system according to claim 51, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

53. The system according to claim 51, wherein results produced by the pharmacoeconomic clinical trials explorer interface are a distinct data/information source which may be used by a second interface in providing reliably appraised data of a desired biological system.

54. The system according to claim 53, wherein the at least two distinct data/information sources are chosen from the group consisting of expert knowledge databases, historical databases, clinical trial results, and computer models.

55. A system for biological data analysis used in developing, testing and evaluating therapies, comprising:

a first interface processing data received from at least one data/information source based upon a first set of parameters defined by a user, wherein the first interface generates results based upon the first set of defined parameters and the at least one data/information source to provide reliably appraised data of a desired biological system;

a second interface processing the results produced by the first interface based upon a second set of parameters defined by a user to provide reliably appraised data of a desired biological system;

wherein the appraised data is applied to develop, test and evaluate therapies relating to the desired biological system.

56. The system according to claim 55, wherein the first interface is a therapy explorer interface processing data to generate results regarding the underlying biology of disease and provide reliably appraised data of the underlying biology of a disease.

57. The system according to claim 56, wherein the second interface is a clinical trials explorer interface processing results generated by the therapy explorer interface to provide a reliable appraisal of the efficacy of specific therapies for a disease.

58. The system according to claim 57, wherein the clinical trials explorer interface generates results based upon a second set of parameters and the results produced by the therapy explorer interface and the system further includes a pharmacoeconomic explorer interface processing results generated by the clinical trials explorer interface based upon a third set of parameters defined by a user to provide reliably appraised data of the effectiveness of a proposed disease treatment when compared to standard therapies.

59. The system according to claim 55, wherein the first interface is a clinical trials explorer interface processing data to generate results regarding the efficacy of specific therapies for a disease and provide reliably appraised data of the efficacy of specific therapies for a disease.

60. The system according to claim 59, wherein the second interface is a pharmacoeconomic explorer interface processing results generated by the clinical tests explorer interface to provide reliably appraised data of the effectiveness of a proposed disease treatment when compared to standard therapies.

61. The system according to claim 55, wherein the second interface generates results based upon a second set of parameters and the results produced by the first explorer, and the system further includes a third interface processing the results produced by the second interface based upon a third set of parameters defined by a user to provide reliably appraised data of a desired biological system.

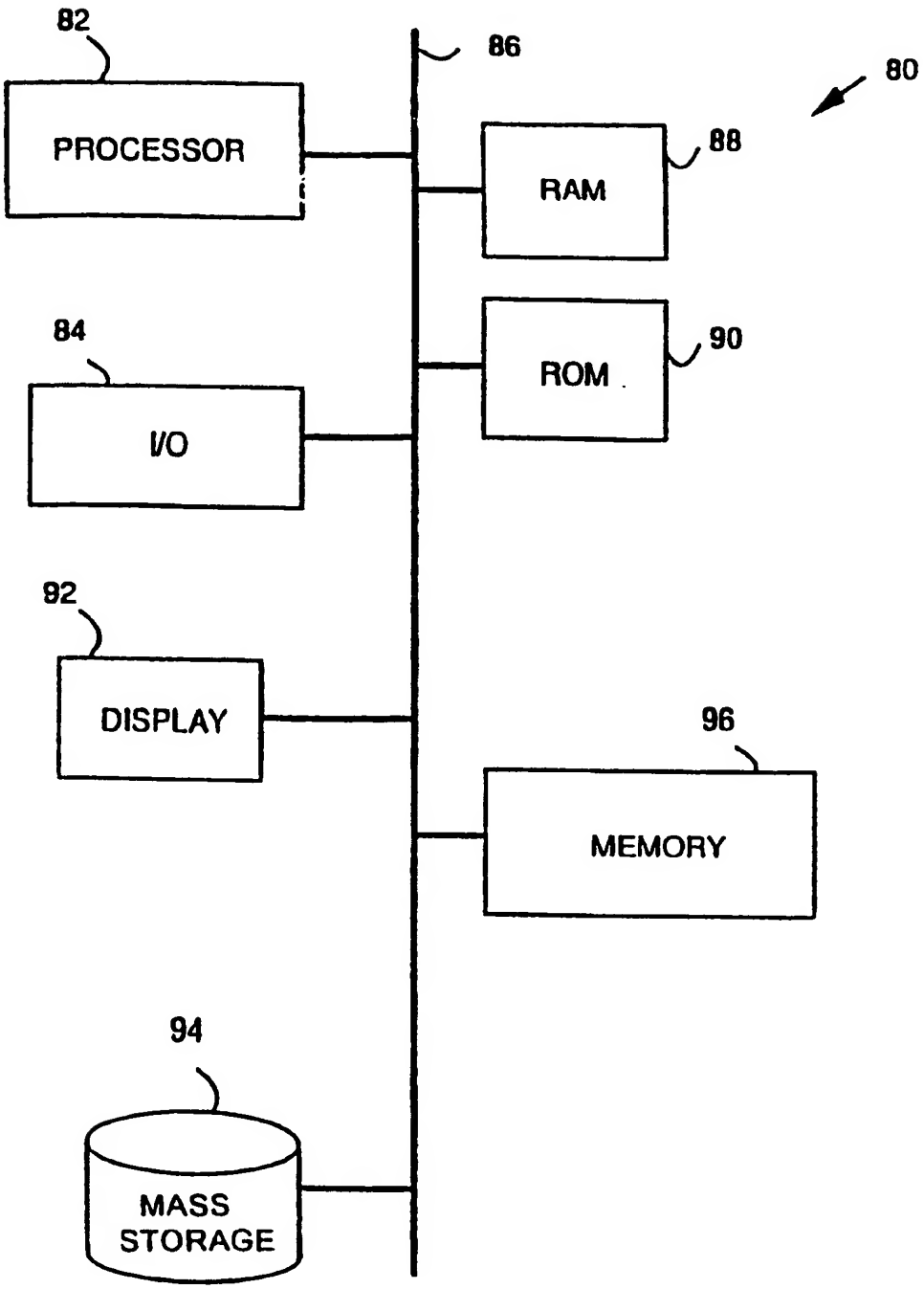
82
PROCESSOR
86
80
88
RAM
84
I/O
90
ROM
92
DISPLAY
96
MEMORY
94
MASS
STORAGE

FIG. 1

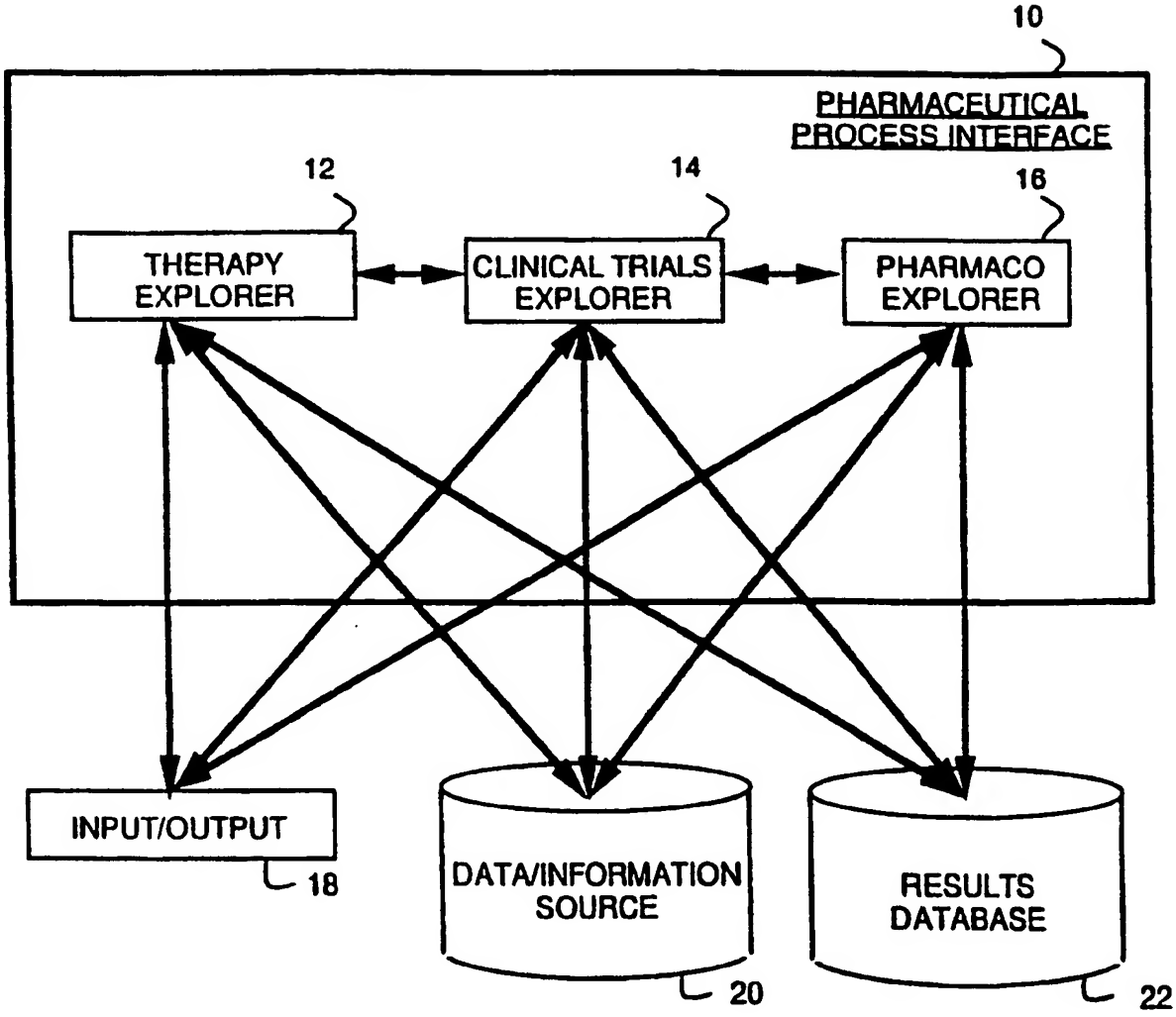
10
PHARMACEUTICAL PROCESS INTERFACE
12
14
16
THERAPY EXPLORER
CLINICAL TRIALS EXPLORER
PHARMACO EXPLORER
INPUT/OUTPUT
18
DATA/INFORMATION SOURCE
20
RESULTS DATABASE
22

FIG. 2

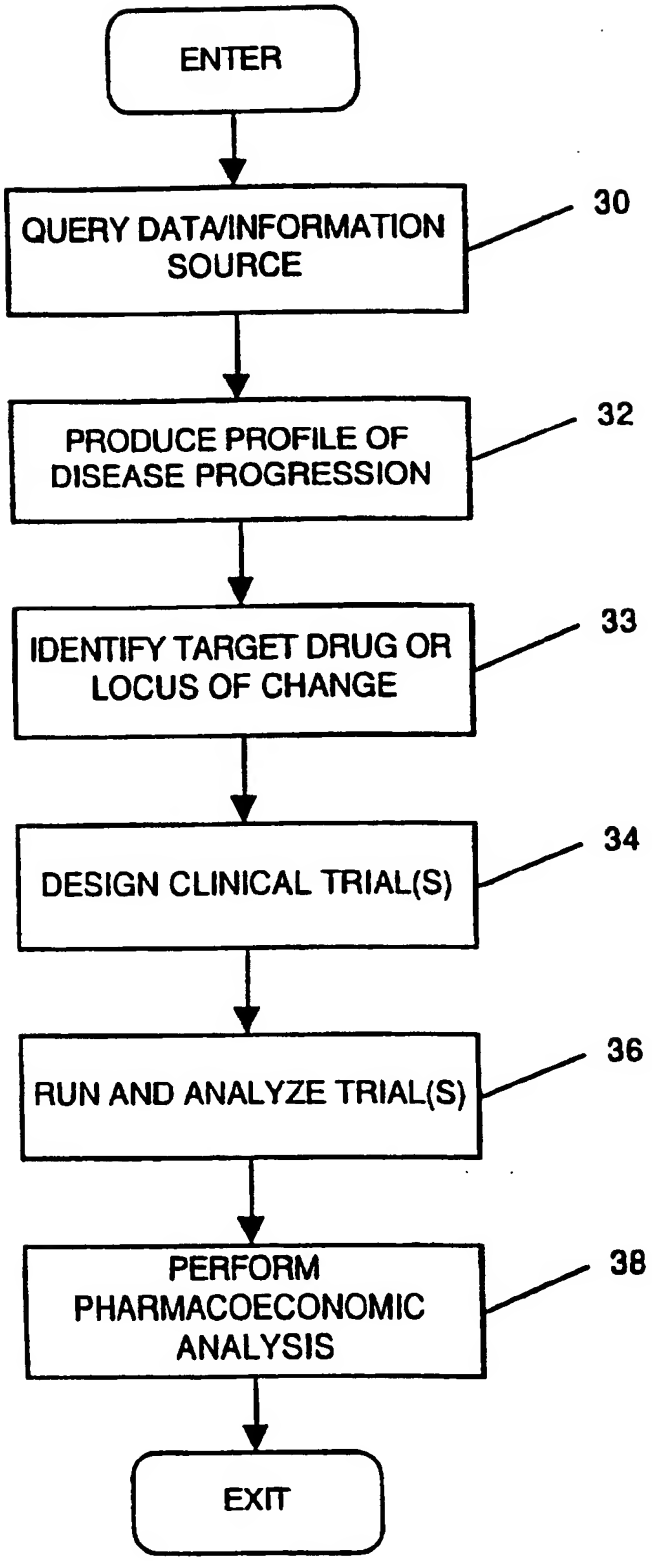
ENTER
QUERY DATA/INFORMATION SOURCE
30
PRODUCE PROFILE OF DISEASE PROGRESSION
32
IDENTIFY TARGET DRUG OR LOCUS OF CHANGE
33
DESIGN CLINICAL TRIAL(S)
34
RUN AND ANALYZE TRIAL(S)
36
PERFORM PHARMACOECONOMIC ANALYSIS
38
EXIT

FIG. 3

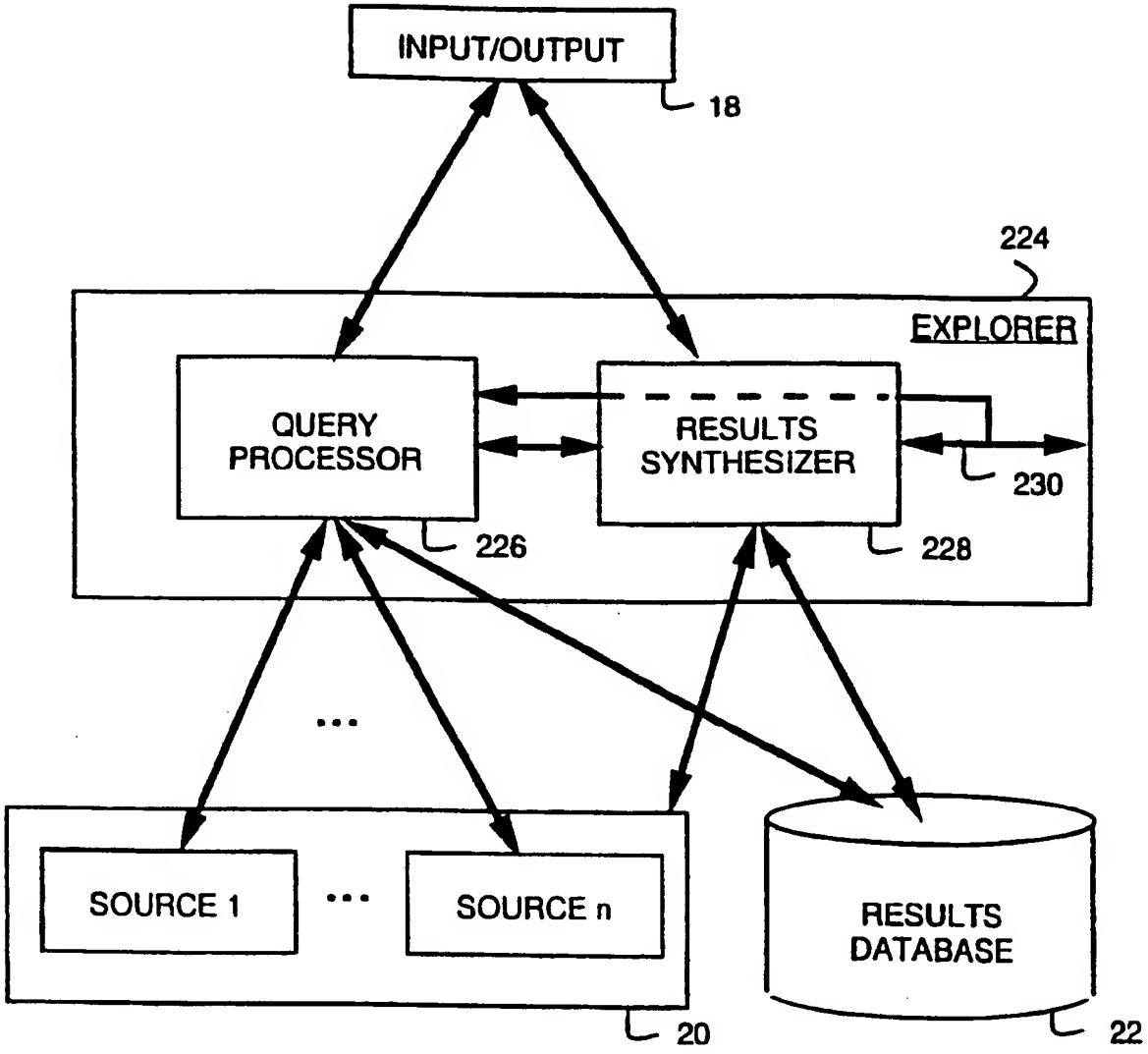
INPUT/OUTPUT
18
224
EXPLORER
QUERY PROCESSOR
RESULTS SYNTHESIZER
230
226
228
SOURCE 1
SOURCE n
RESULTS DATABASE
20
22

FIG. 4

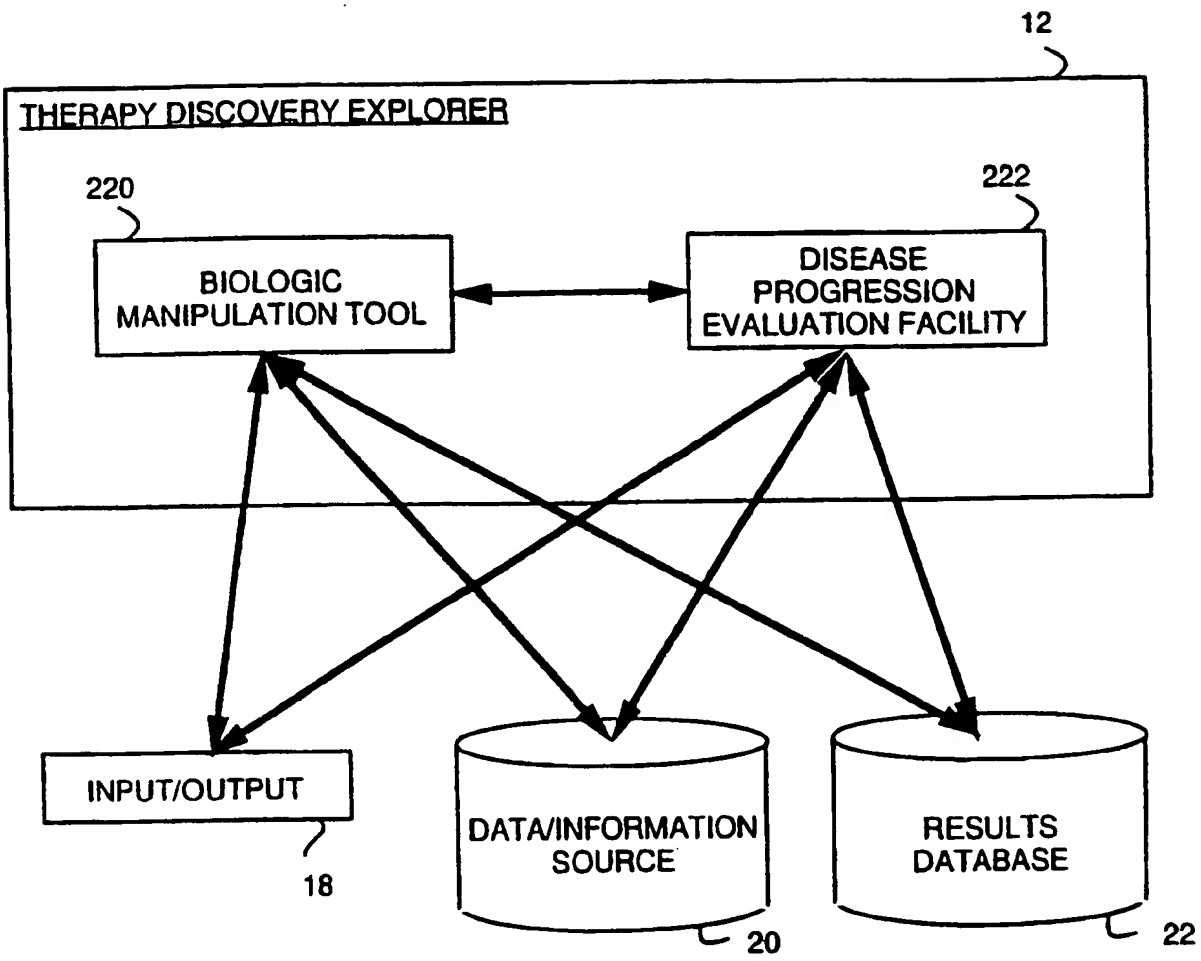
12
THERAPY DISCOVERY EXPLORER
220
222
BIOLOGIC MANIPULATION TOOL
DISEASE PROGRESSION EVALUATION FACILITY
INPUT/OUTPUT
18
DATA/INFORMATION SOURCE
20
RESULTS DATABASE
22

FIG. 5

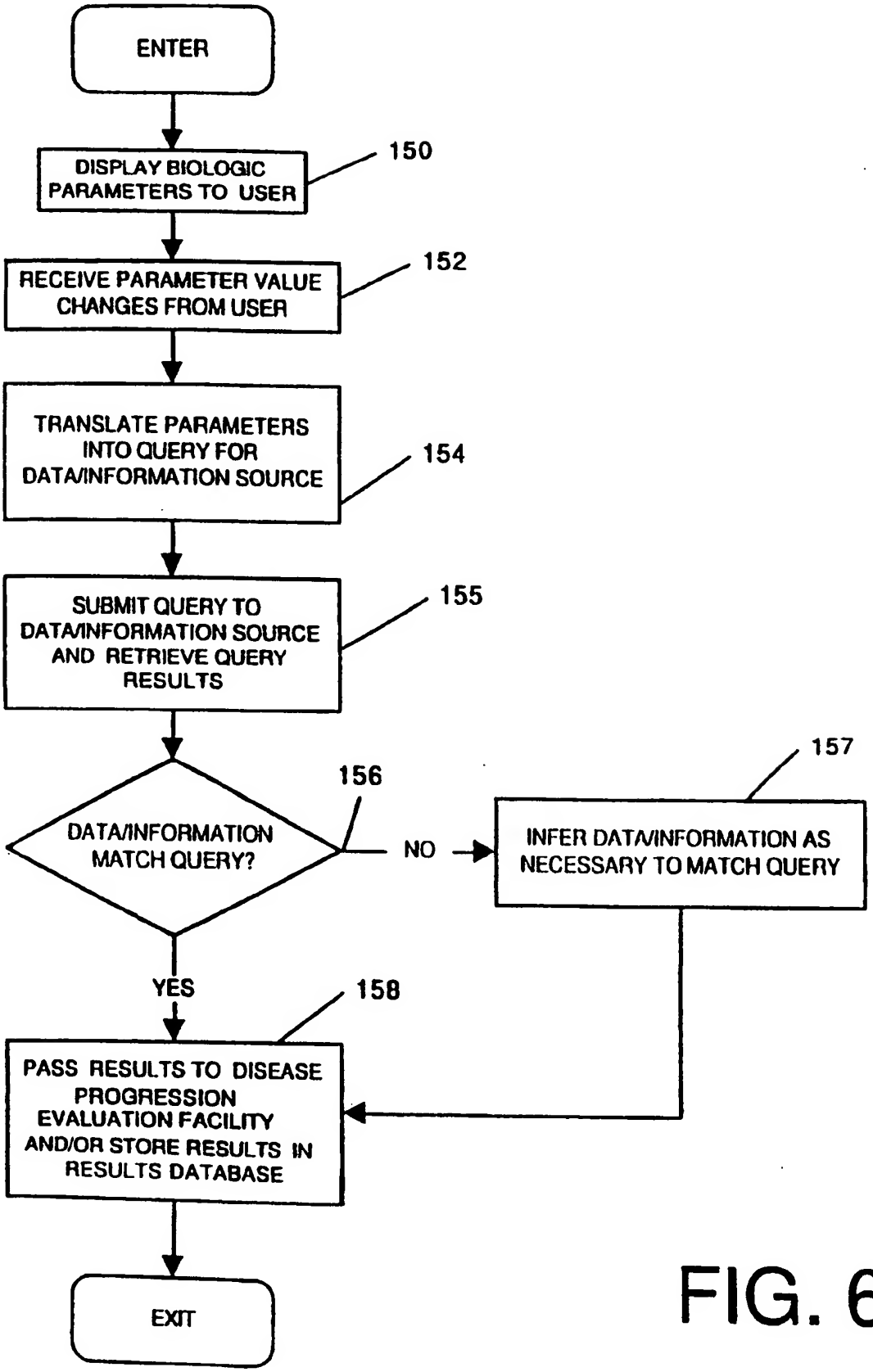
ENTER
DISPLAY BIOLOGIC PARAMETERS TO USER
150
RECEIVE PARAMETER VALUE CHANGES FROM USER
152
TRANSLATE PARAMETERS INTO QUERY FOR DATA/INFORMATION SOURCE
154
SUBMIT QUERY TO DATA/INFORMATION SOURCE AND RETRIEVE QUERY RESULTS
155
DATA/INFORMATION MATCH QUERY?
156
NO
INFER DATA/INFORMATION AS NECESSARY TO MATCH QUERY
157
YES
158
PASS RESULTS TO DISEASE PROGRESSION EVALUATION FACILITY AND/OR STORE RESULTS IN RESULTS DATABASE
EXIT

FIG. 6

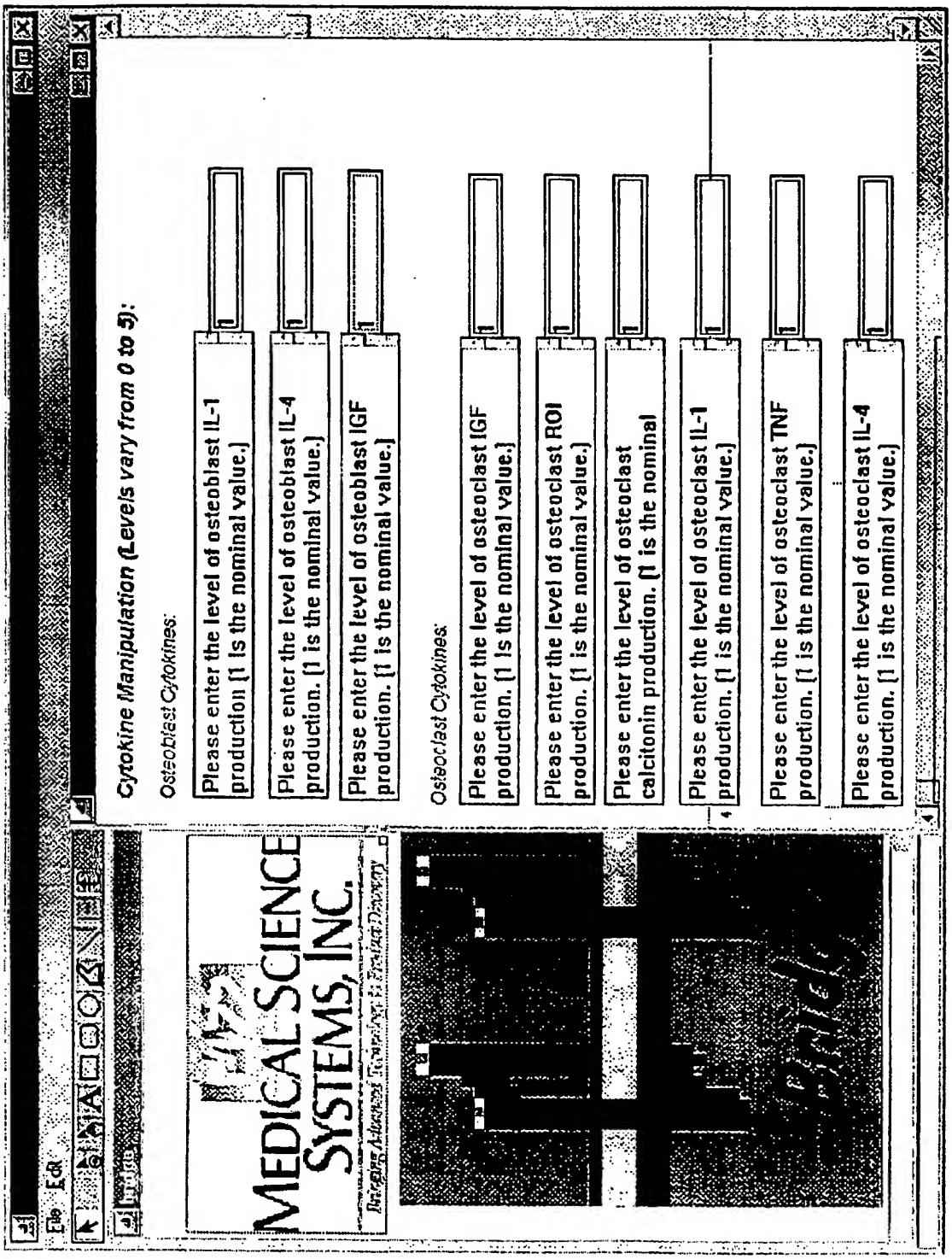
File Edit
MEDICAL SCIENCE SYSTEMS, INC.
Cytokine Manipulation (Levels vary from 0 to 5):
Osteoblast Cytokines:
Please enter the level of osteoblast IL-1 production (1 is the nominal value.)
Please enter the level of osteoblast IL-4 production. (1 is the nominal value.)
Please enter the level of osteoblast IGF production. (1 is the nominal value.)
Osteoclast Cytokines:
Please enter the level of osteoclast IGF production. (1 is the nominal value.)
Please enter the level of osteoclast ROI production. (1 is the nominal value.)
Please enter the level of osteoclast calcitonin production. (1 is the nominal
Please enter the level of osteoclast IL-1 production. (1 is the nominal value.)
Please enter the level of osteoclast TNF production. (1 is the nominal value.)
Please enter the level of osteoclast IL-4 production. (1 is the nominal value.)

FIG. 7

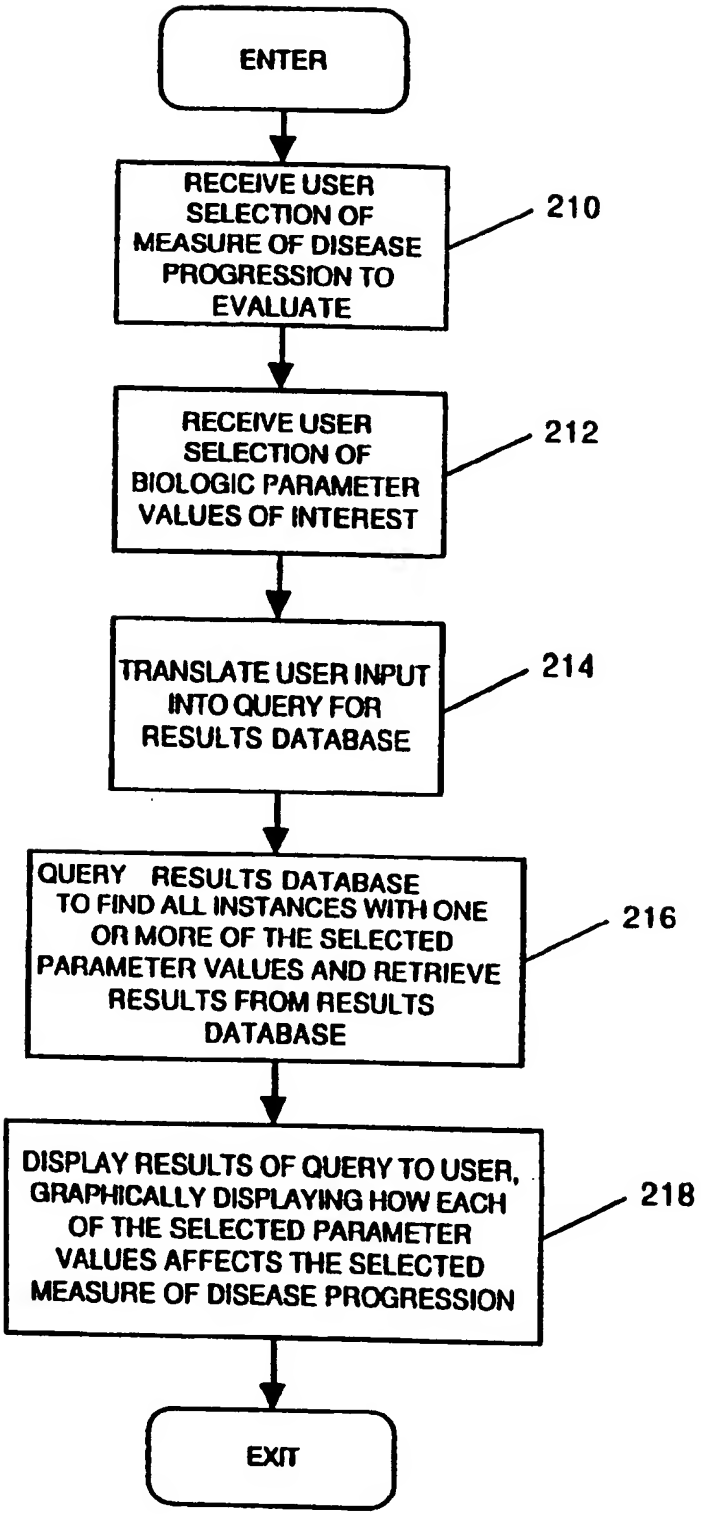
ENTER
RECEIVE USER SELECTION OF MEASURE OF DISEASE PROGRESSION TO EVALUATE
210
RECEIVE USER SELECTION OF BIOLOGIC PARAMETER VALUES OF INTEREST
212
TRANSLATE USER INPUT INTO QUERY FOR RESULTS DATABASE
214
QUERY RESULTS DATABASE TO FIND ALL INSTANCES WITH ONE OR MORE OF THE SELECTED PARAMETER VALUES AND RETRIEVE RESULTS FROM RESULTS DATABASE
216
DISPLAY RESULTS OF QUERY TO USER, GRAPHICALLY DISPLAYING HOW EACH OF THE SELECTED PARAMETER VALUES AFFECTS THE SELECTED MEASURE OF DISEASE PROGRESSION
218
EXIT

FIG. 8

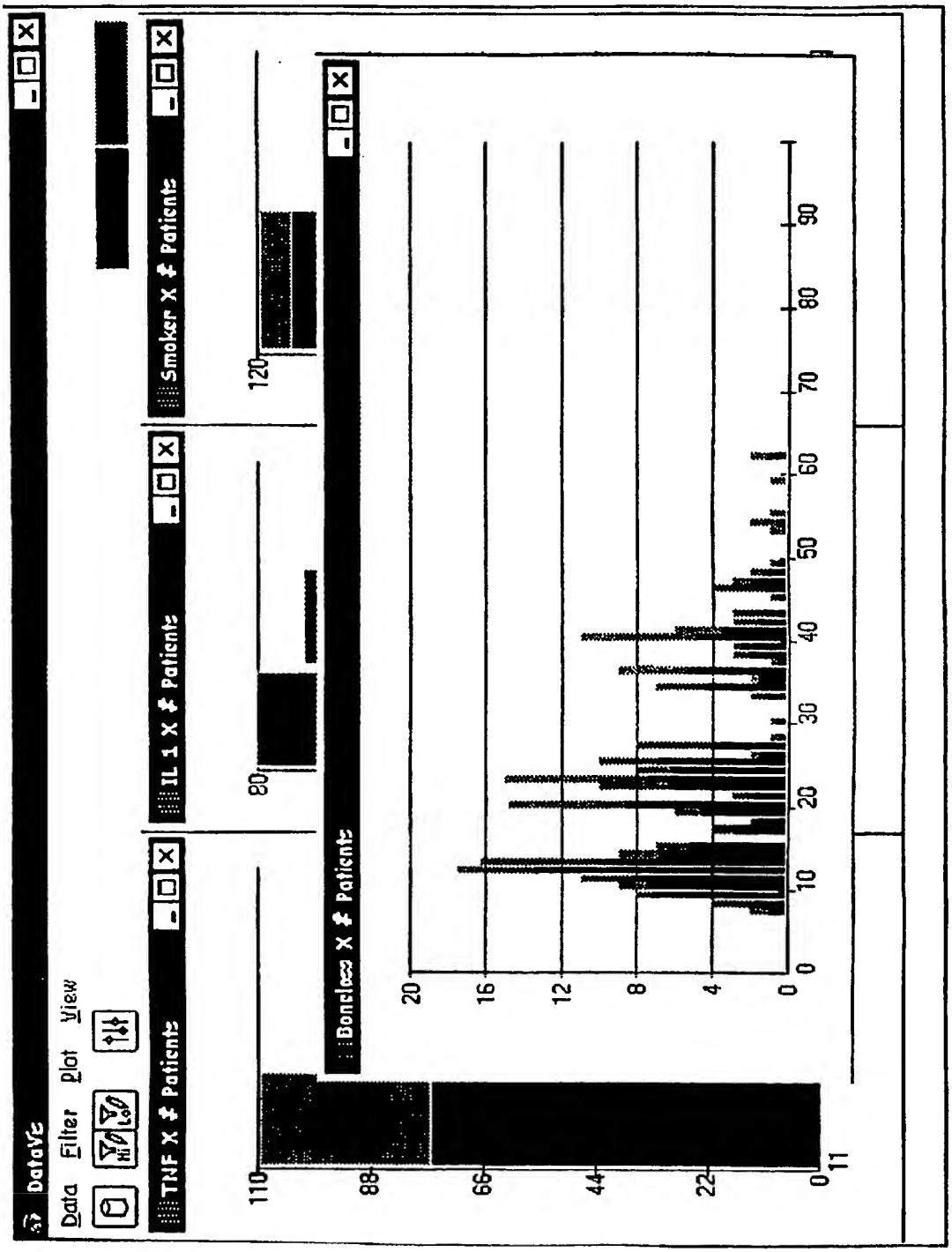
DataVe
Data Filter Plot View
TNF X # Patients
IL 1 X # Patients
Smoker X # Patients
Boneless X # Patients
110
88
66
44
22
0
11
80
120
20
16
12
8
4
0
0
10
20
30
40
50
60
70
80
90

FIG. 9

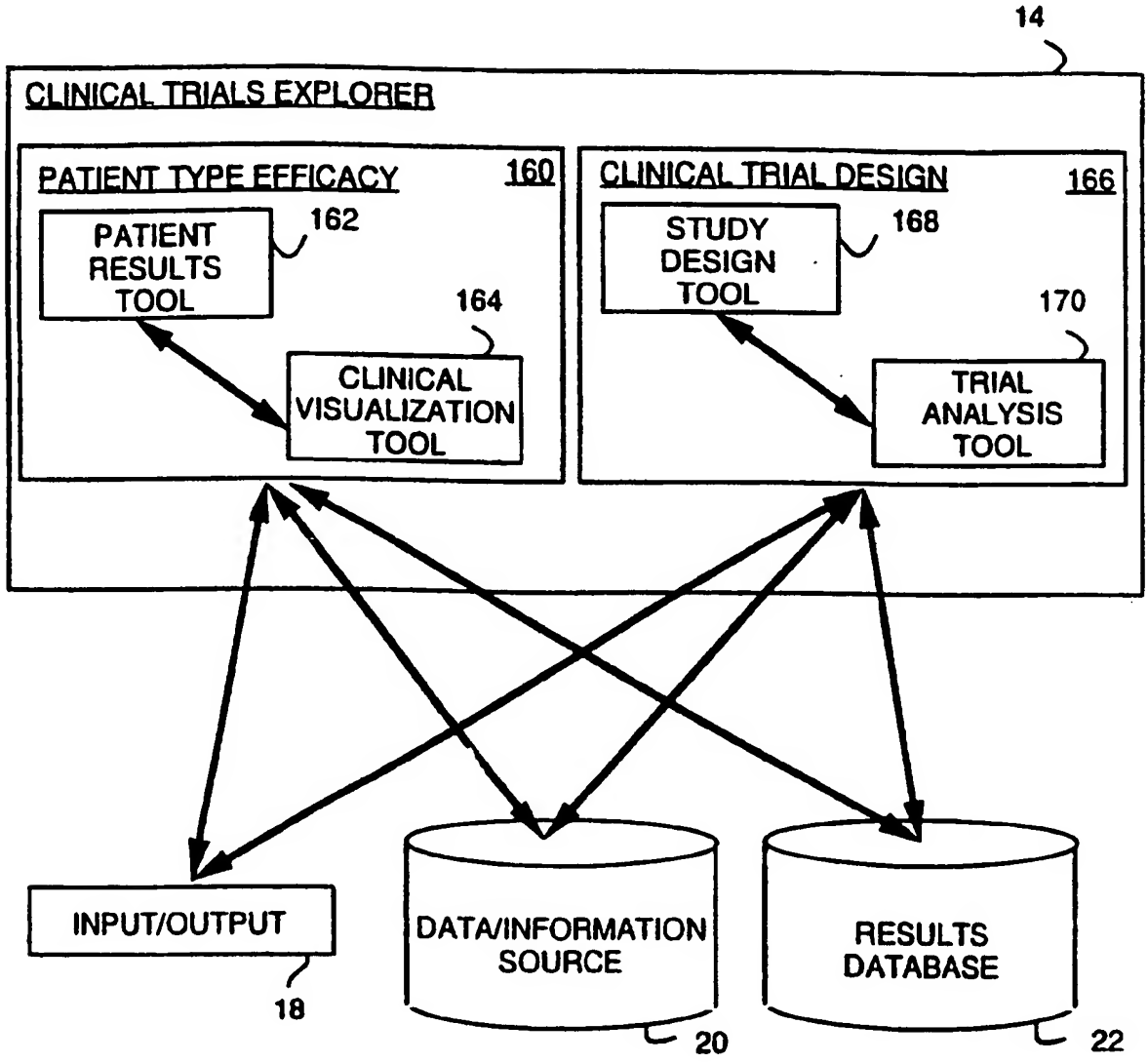
14
CLINICAL TRIALS EXPLORER
PATIENT TYPE EFFICACY
160
PATIENT RESULTS TOOL
162
164
CLINICAL VISUALIZATION TOOL
CLINICAL TRIAL DESIGN
166
STUDY DESIGN TOOL
168
170
TRIAL ANALYSIS TOOL
INPUT/OUTPUT
18
DATA/INFORMATION SOURCE
20
RESULTS DATABASE
22

FIG. 10

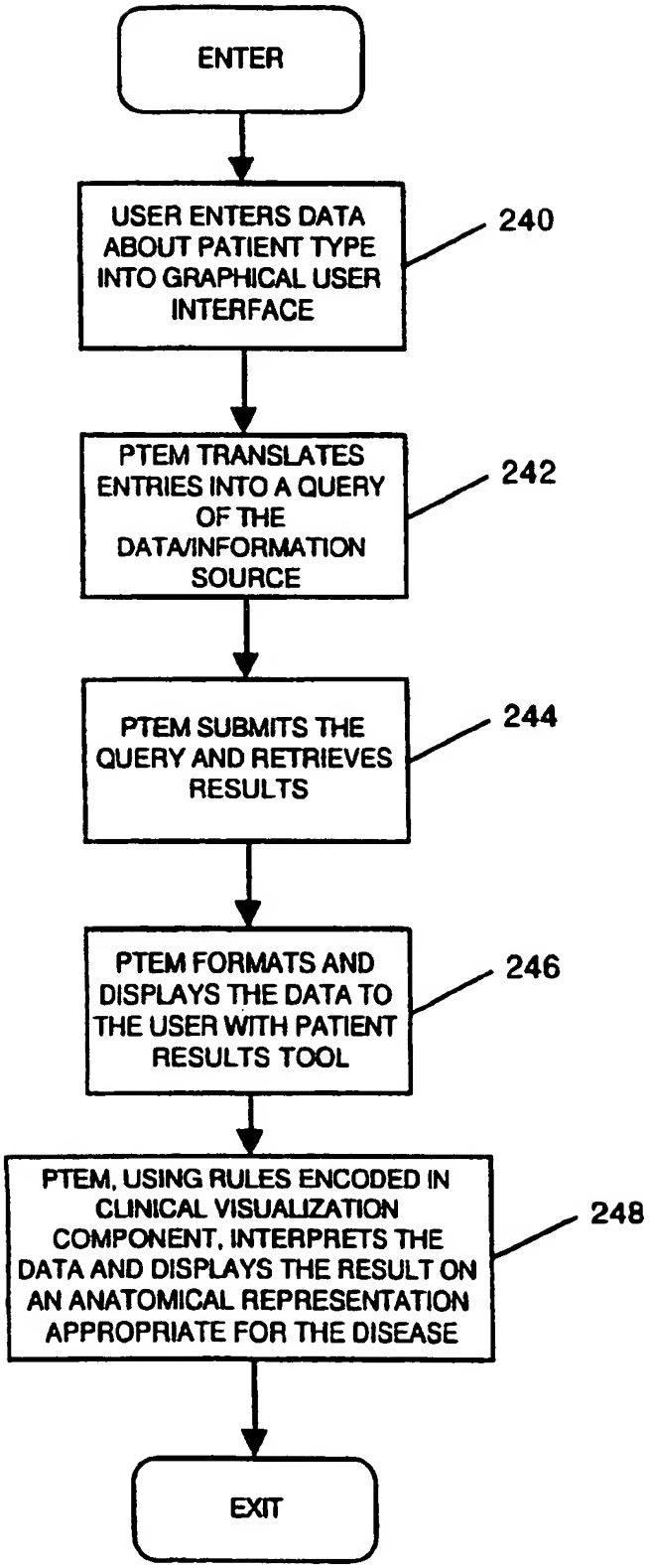
ENTER
USER ENTERS DATA ABOUT PATIENT TYPE INTO GRAPHICAL USER INTERFACE
240
PTEM TRANSLATES ENTRIES INTO A QUERY OF THE DATA/INFORMATION SOURCE
242
PTEM SUBMITS THE QUERY AND RETRIEVES RESULTS
244
PTEM FORMATS AND DISPLAYS THE DATA TO THE USER WITH PATIENT RESULTS TOOL
246
PTEM, USING RULES ENCODED IN CLINICAL VISUALIZATION COMPONENT, INTERPRETS THE DATA AND DISPLAYS THE RESULT ON AN ANATOMICAL REPRESENTATION APPROPRIATE FOR THE DISEASE
248
EXIT

FIG. 11

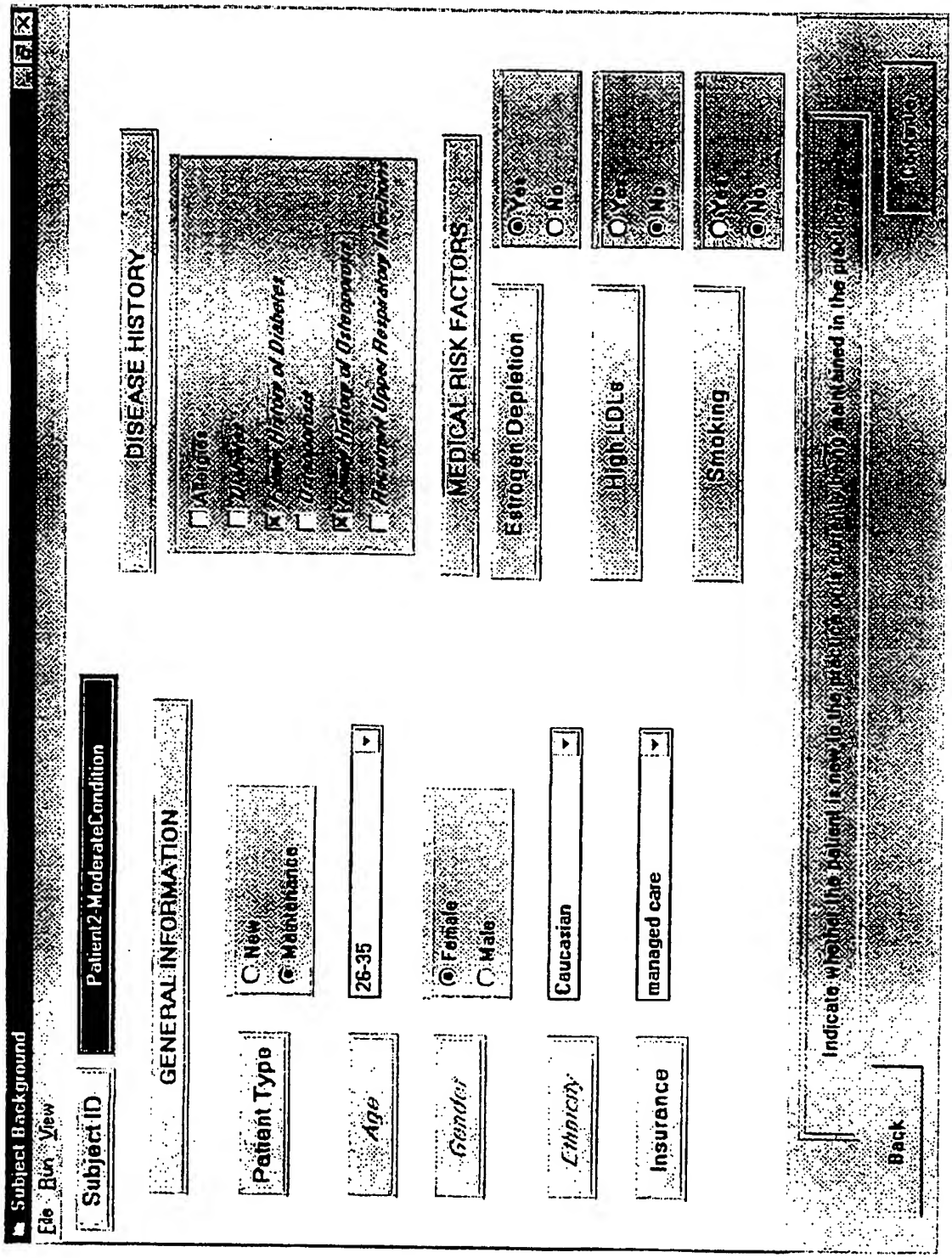
Subject Background
File Run View
Subject ID
Patient2 ModerateCondition
GENERAL INFORMATION
Patient Type
New
Maintenance
Age
26-35
Gender
Female
Male
Ethnicity
Caucasian
Insurance
managed care
DISEASE HISTORY
Abortion
Diabetes
Family History of Diabetes
Osteoporosis
Family History of Osteoporosis
Treatment Upon Respiratory Infection
MEDICAL RISK FACTORS
Estrogen Depletion
Yes
No
High LDLs
Yes
No
Smoking
Yes
No
Indicate whether the patient is new to the practice or maintained in the practice
Back
Continue

FIG. 12

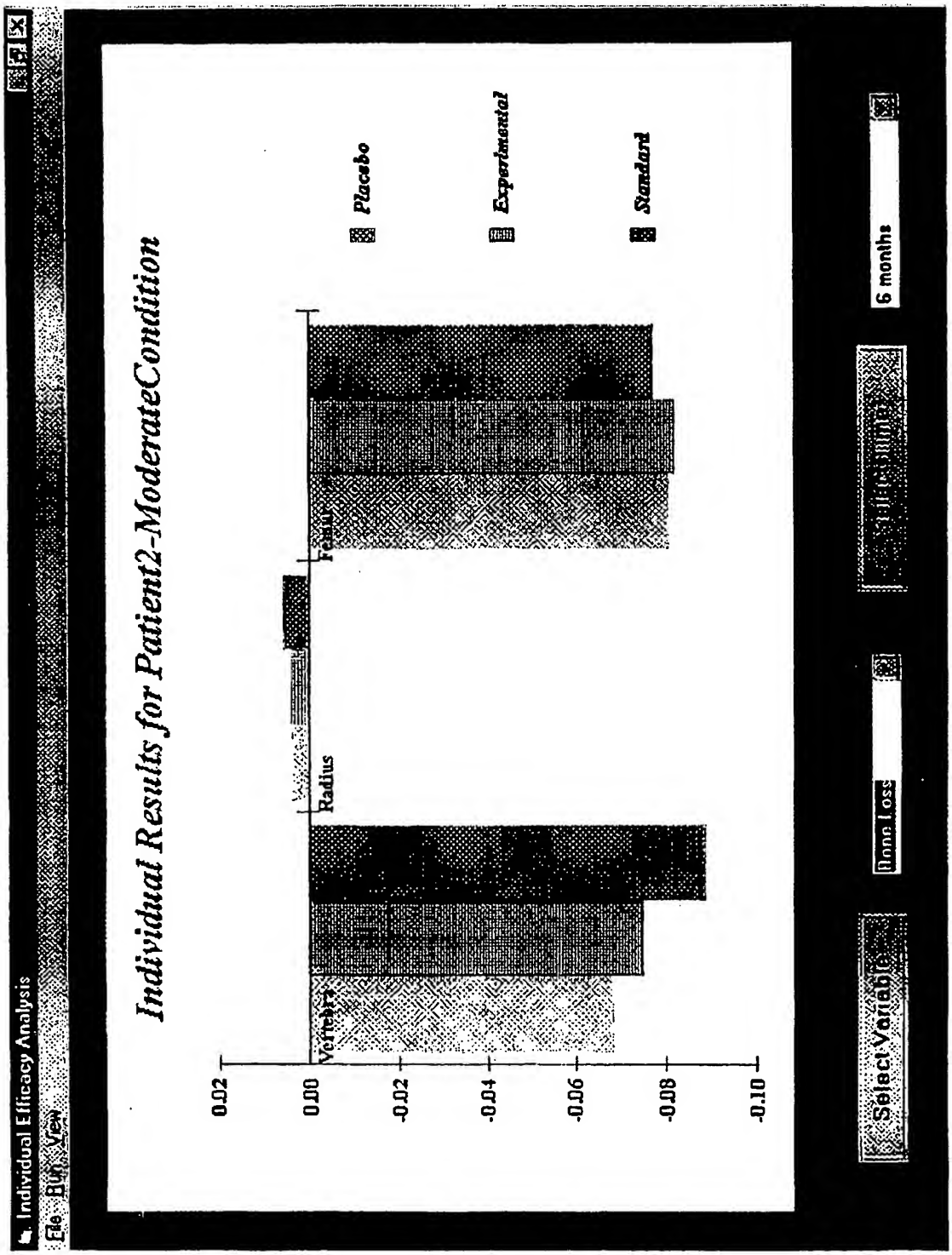
Individual Efficacy Analysis
File Run View
Individual Results for Patient2-ModerateCondition
Placebo
Experimental
Standard
Radius
Vertebra
0.02
0.00
-0.02
-0.04
-0.06
-0.08
-0.10
Select Variable
Bone Loss
6 months

FIG. 13

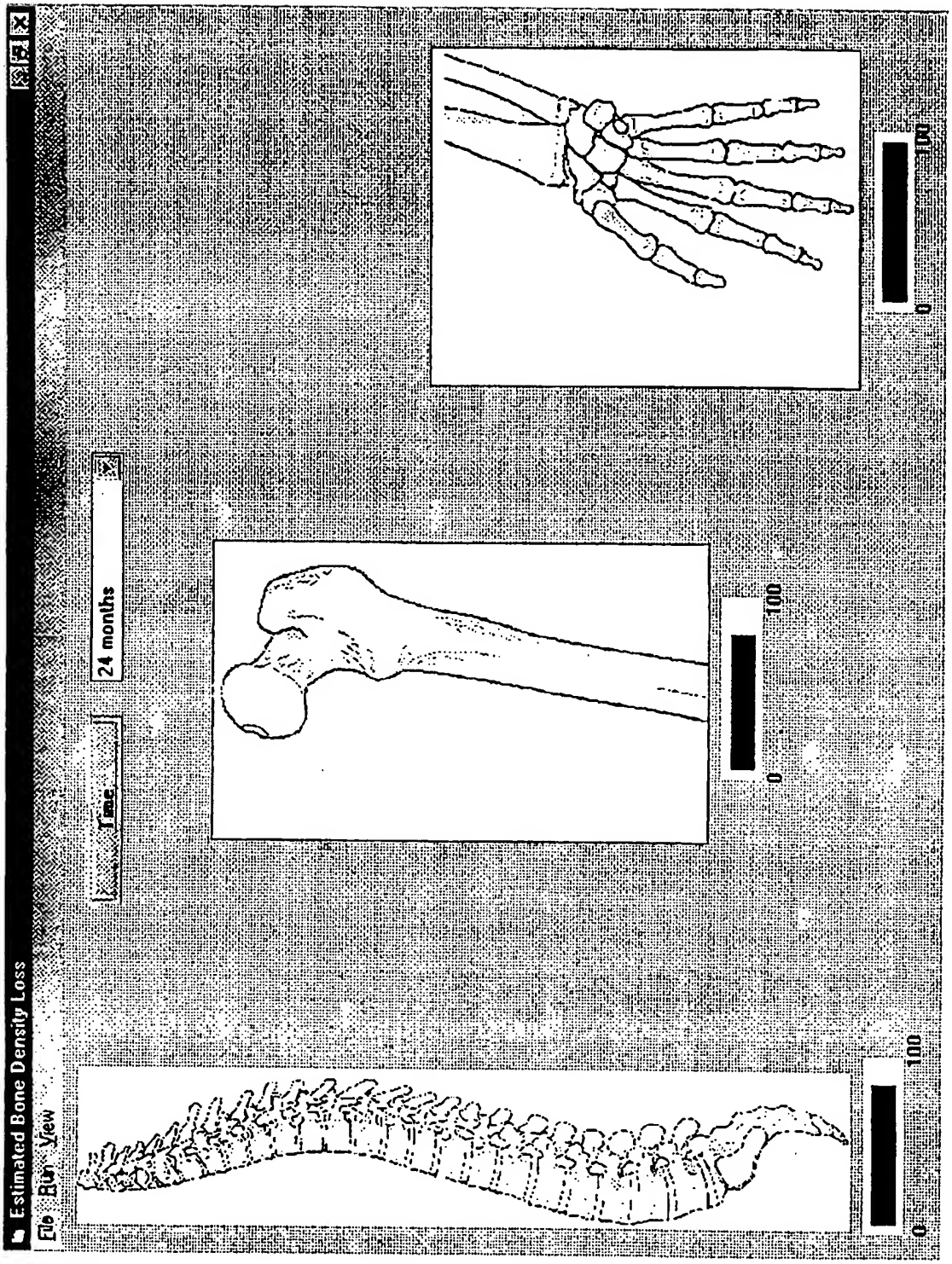
Estimated Bone Density Loss
File Run View
Time
24 months
100
0
100
0
100
0

FIG. 14

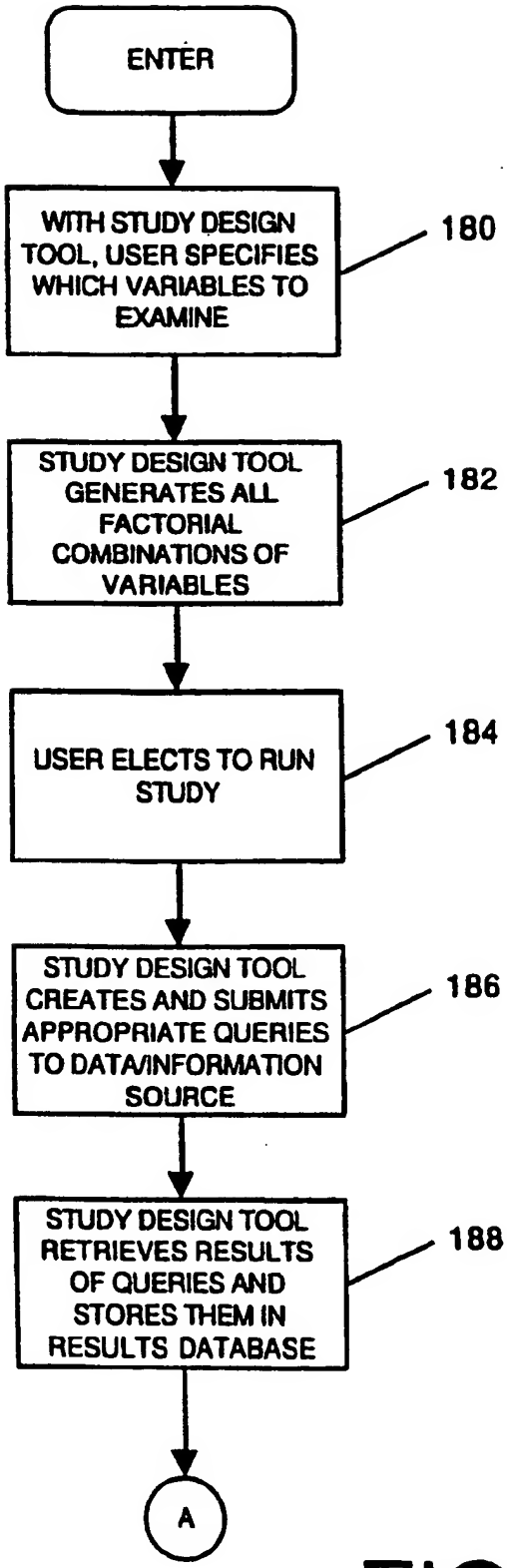
ENTER
WITH STUDY DESIGN TOOL, USER SPECIFIES WHICH VARIABLES TO EXAMINE
180
STUDY DESIGN TOOL GENERATES ALL FACTORIAL COMBINATIONS OF VARIABLES
182
USER ELECTS TO RUN STUDY
184
STUDY DESIGN TOOL CREATES AND SUBMITS APPROPRIATE QUERIES TO DATA/INFORMATION SOURCE
186
STUDY DESIGN TOOL RETRIEVES RESULTS OF QUERIES AND STORES THEM IN RESULTS DATABASE
188
A

FIG. 15a

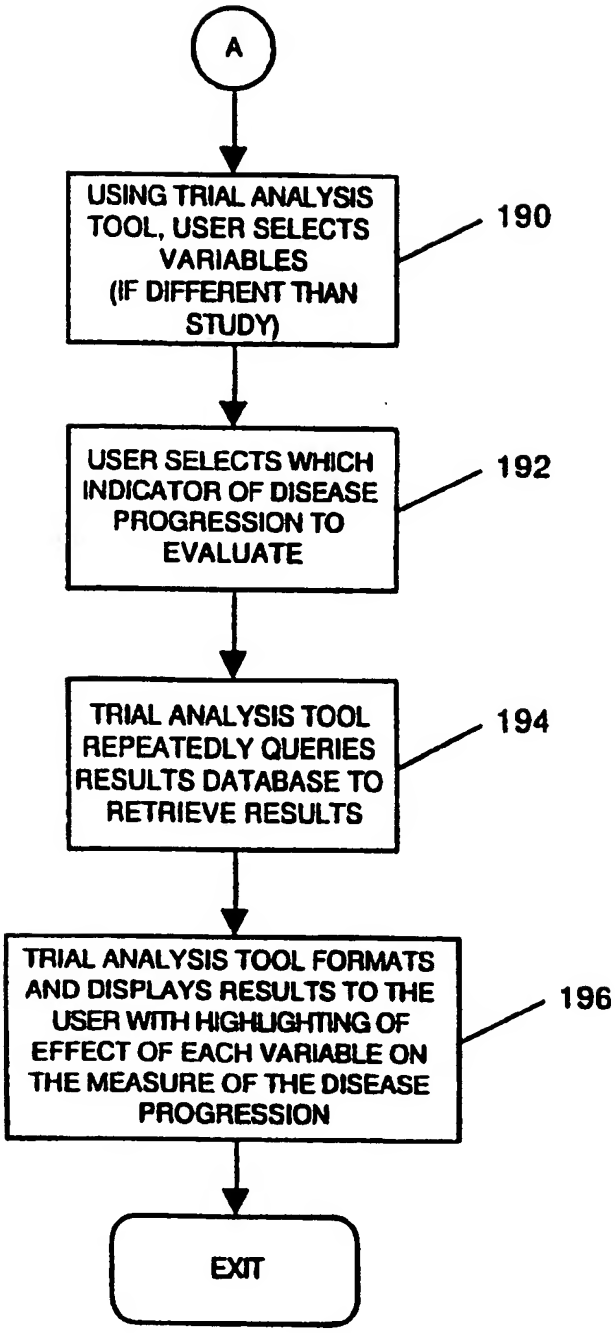
A
USING TRIAL ANALYSIS TOOL, USER SELECTS VARIABLES (IF DIFFERENT THAN STUDY)
190
USER SELECTS WHICH INDICATOR OF DISEASE PROGRESSION TO EVALUATE
192
TRIAL ANALYSIS TOOL REPEATEDLY QUERIES RESULTS DATABASE TO RETRIEVE RESULTS
194
TRIAL ANALYSIS TOOL FORMATS AND DISPLAYS RESULTS TO THE USER WITH HIGHLIGHTING OF EFFECT OF EACH VARIABLE ON THE MEASURE OF THE DISEASE PROGRESSION
196
EXIT

FIG. 15b

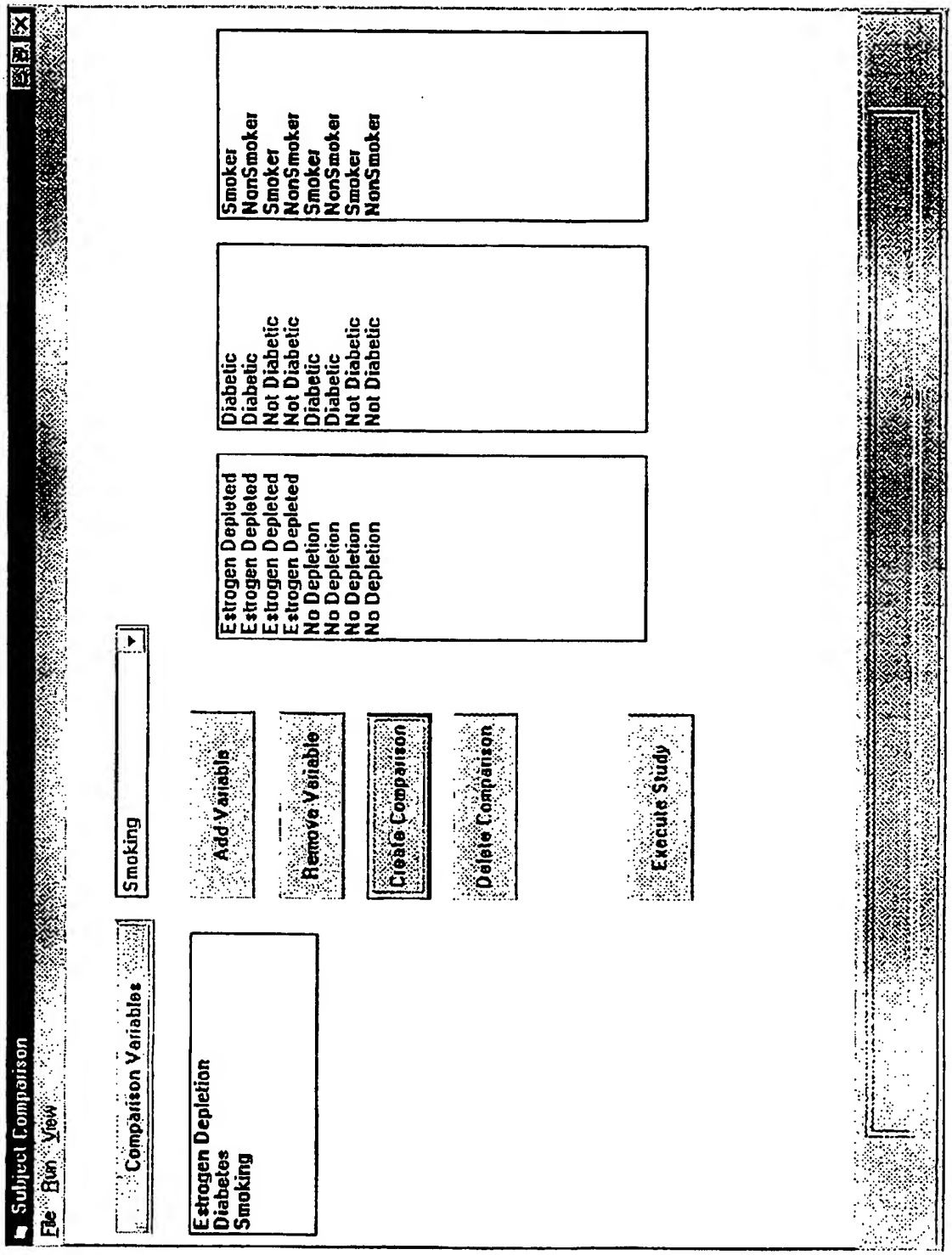
Subject Comparison
File Run View
Comparison Variables
Estrogen Depletion
Diabetes
Smoking
Smoking
Add Variable
Remove Variable
Create Comparison
Delete Comparison
Execute Study
Estrogen Depleted
Estrogen Depleted
Estrogen Depleted
Estrogen Depleted
No Depletion
No Depletion
No Depletion
No Depletion
Diabetic
Diabetic
Not Diabetic
Not Diabetic
Diabetic
Diabetic
Not Diabetic
Not Diabetic
Smoker
NonSmoker
Smoker
NonSmoker
Smoker
NonSmoker
Smoker
NonSmoker

FIG. 16

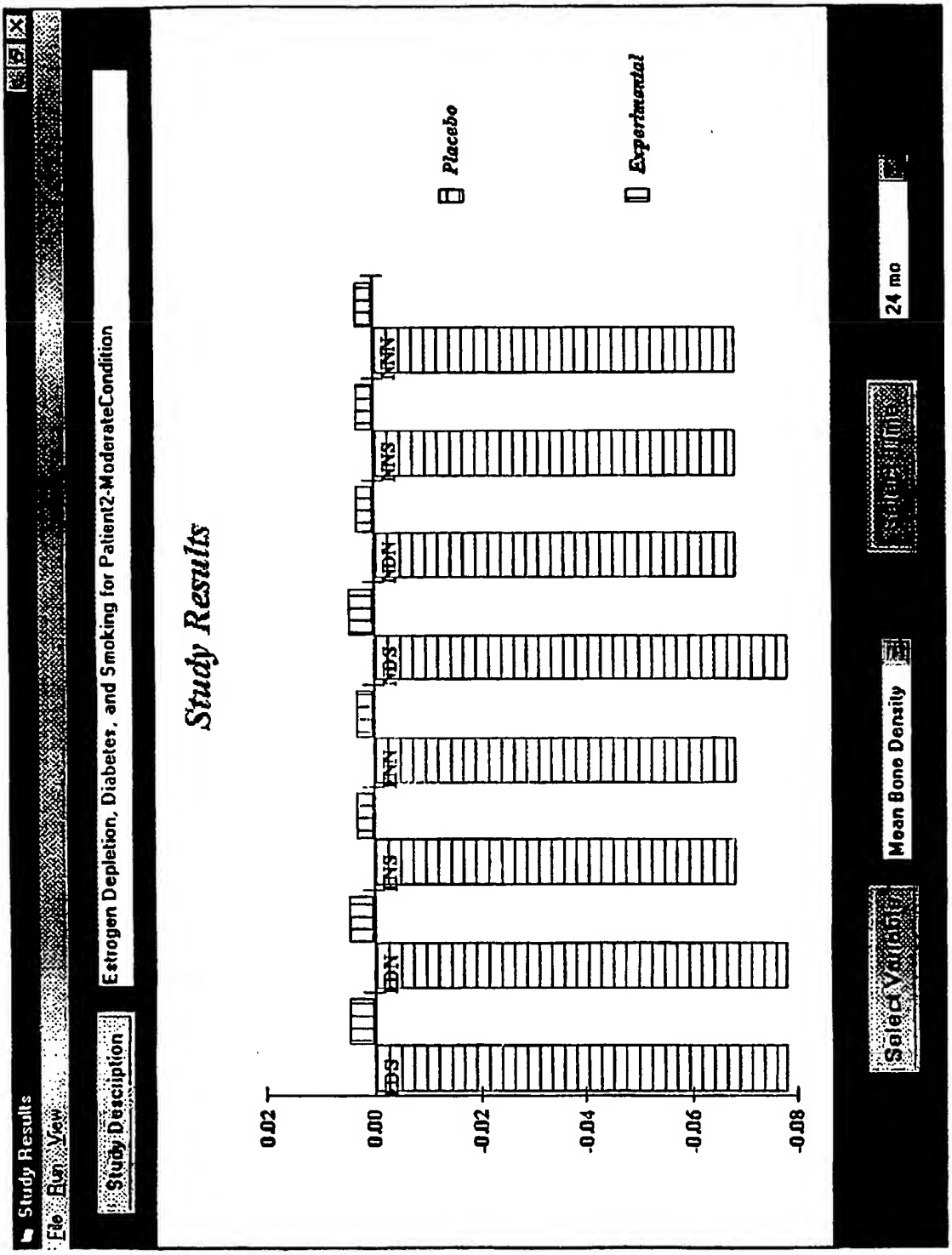
Study Results
File Run View
Study Description
Estrogen Depletion, Diabetes, and Smoking for Patient2-ModerateCondition
Study Results
Placebo
Experimental
0.02
0.00
-0.02
-0.04
-0.06
-0.08
EDS
EDN
ENS
ENN
NDS
NDN
NNS
NNN
Select Variable
Mean Bone Density
24 mo

FIG. 17

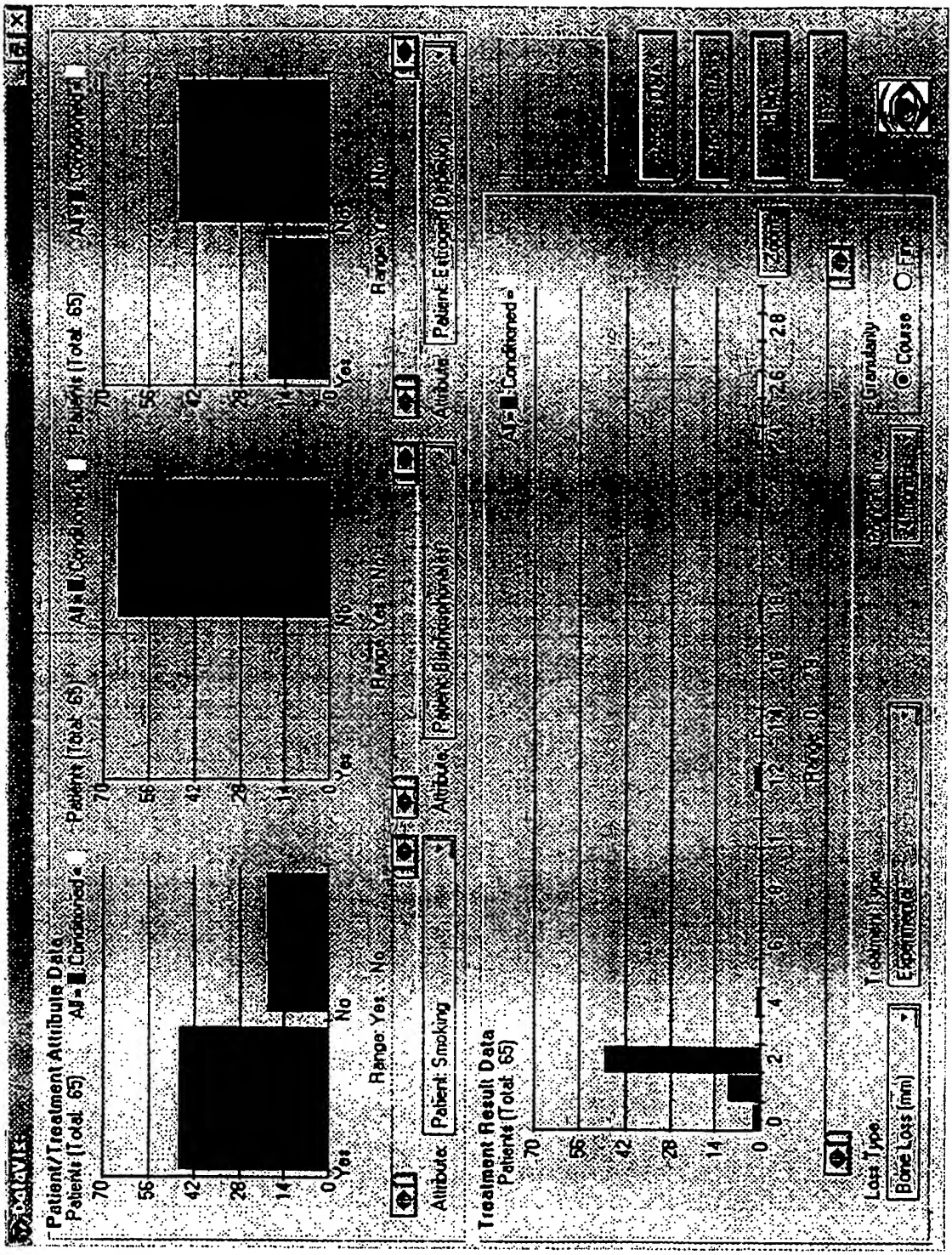
Patient/Treatment Attribute Data
Patients (Total: 65)
Attribute
Patient Smoking
Range Yes
Range No
Patient Diabetic
Treatment Result Data
Patients (Total: 65)
Bone Loss (mm)
Loss Type
Course
Granulary

FIG. 18

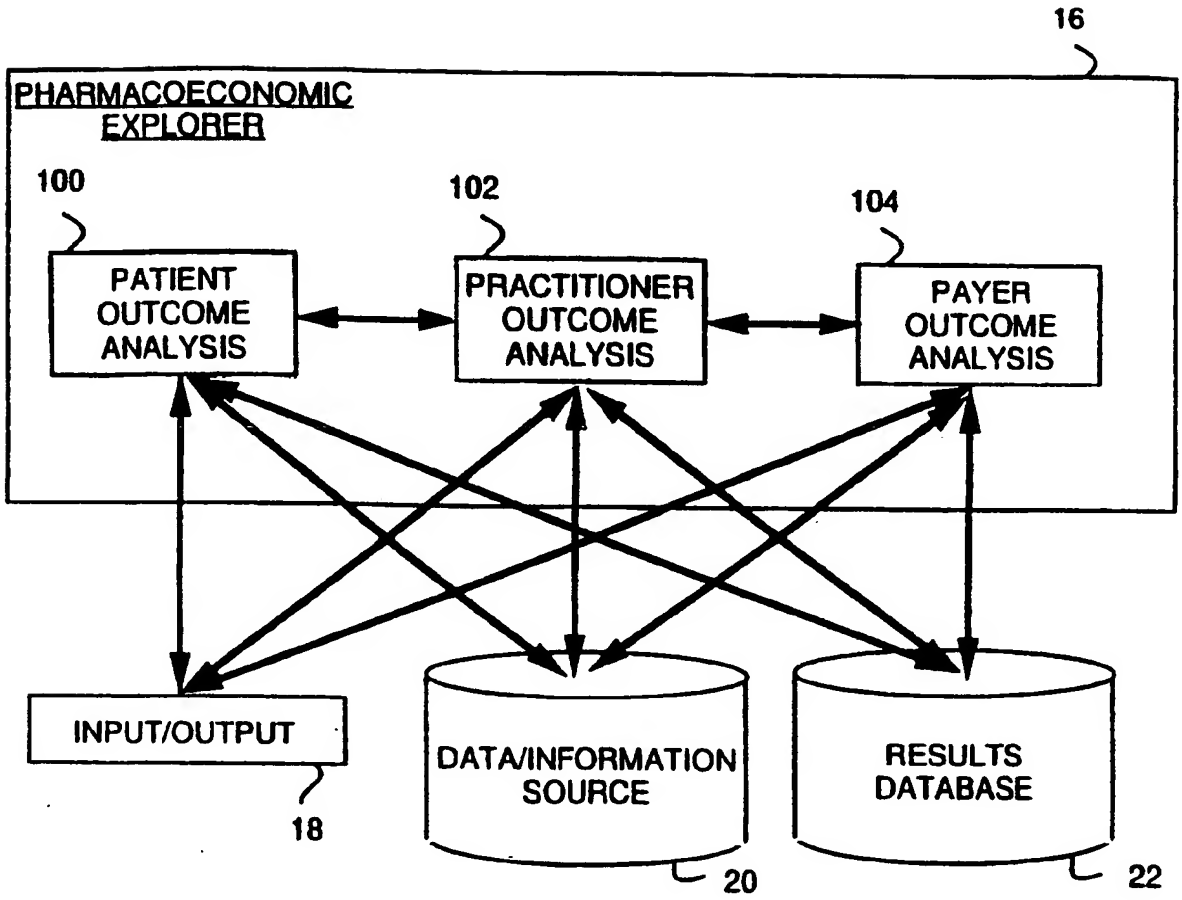
16
PHARMACOECONOMIC EXPLORER
100
102
104
PATIENT OUTCOME ANALYSIS
PRACTITIONER OUTCOME ANALYSIS
PAYER OUTCOME ANALYSIS
INPUT/OUTPUT
18
DATA/INFORMATION SOURCE
20
RESULTS DATABASE
22

FIG. 19

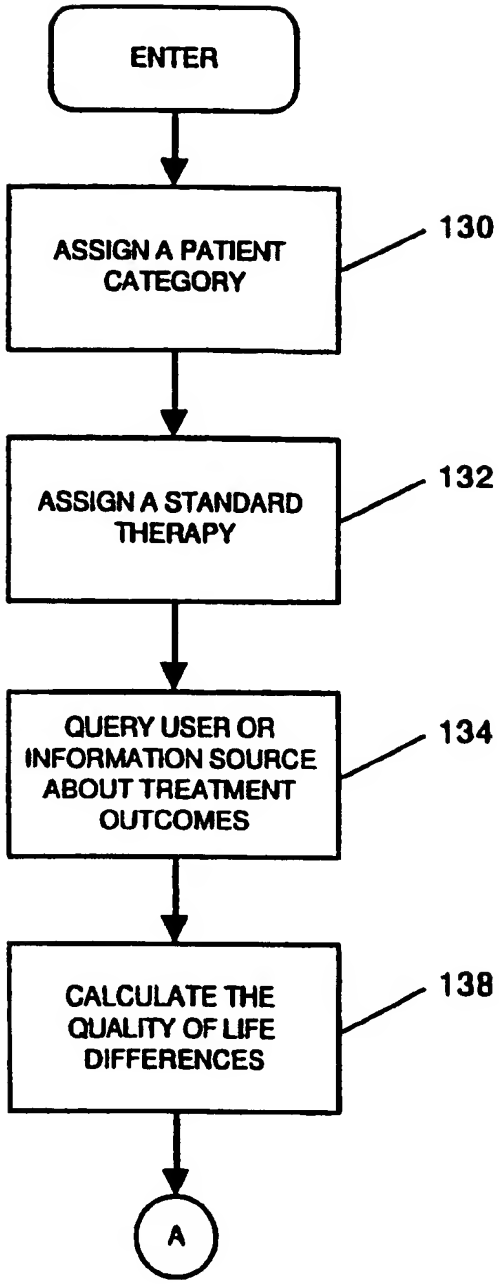
ENTER
ASSIGN A PATIENT CATEGORY
130
ASSIGN A STANDARD THERAPY
132
QUERY USER OR INFORMATION SOURCE ABOUT TREATMENT OUTCOMES
134
CALCULATE THE QUALITY OF LIFE DIFFERENCES
138
A

FIG. 20a

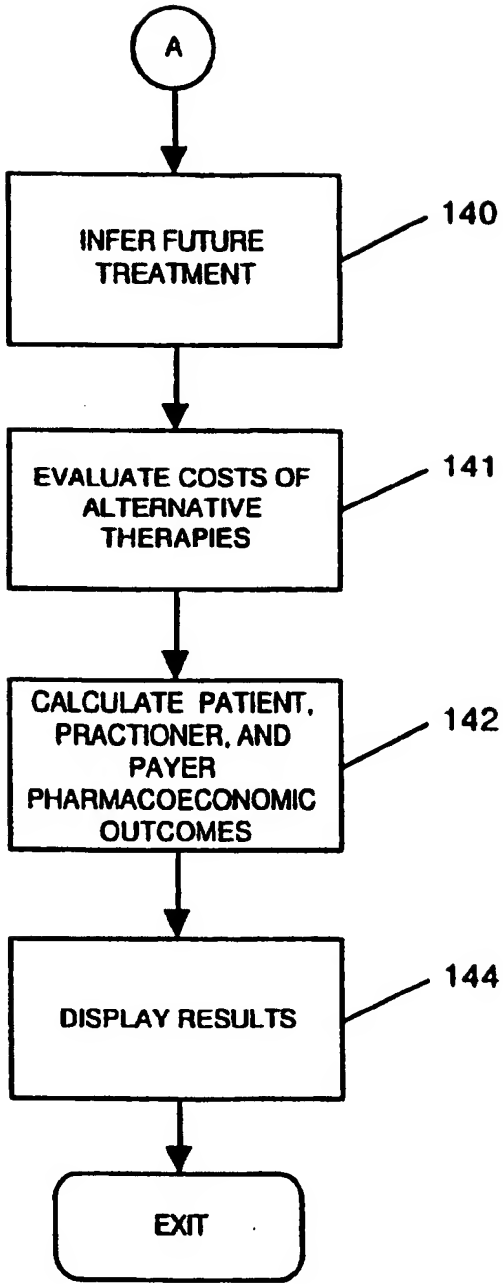
A
INFER FUTURE TREATMENT
140
EVALUATE COSTS OF ALTERNATIVE THERAPIES
141
CALCULATE PATIENT, PRACTIONER, AND PAYER PHARMACOECONOMIC OUTCOMES
142
DISPLAY RESULTS
144
EXIT

FIG. 20b

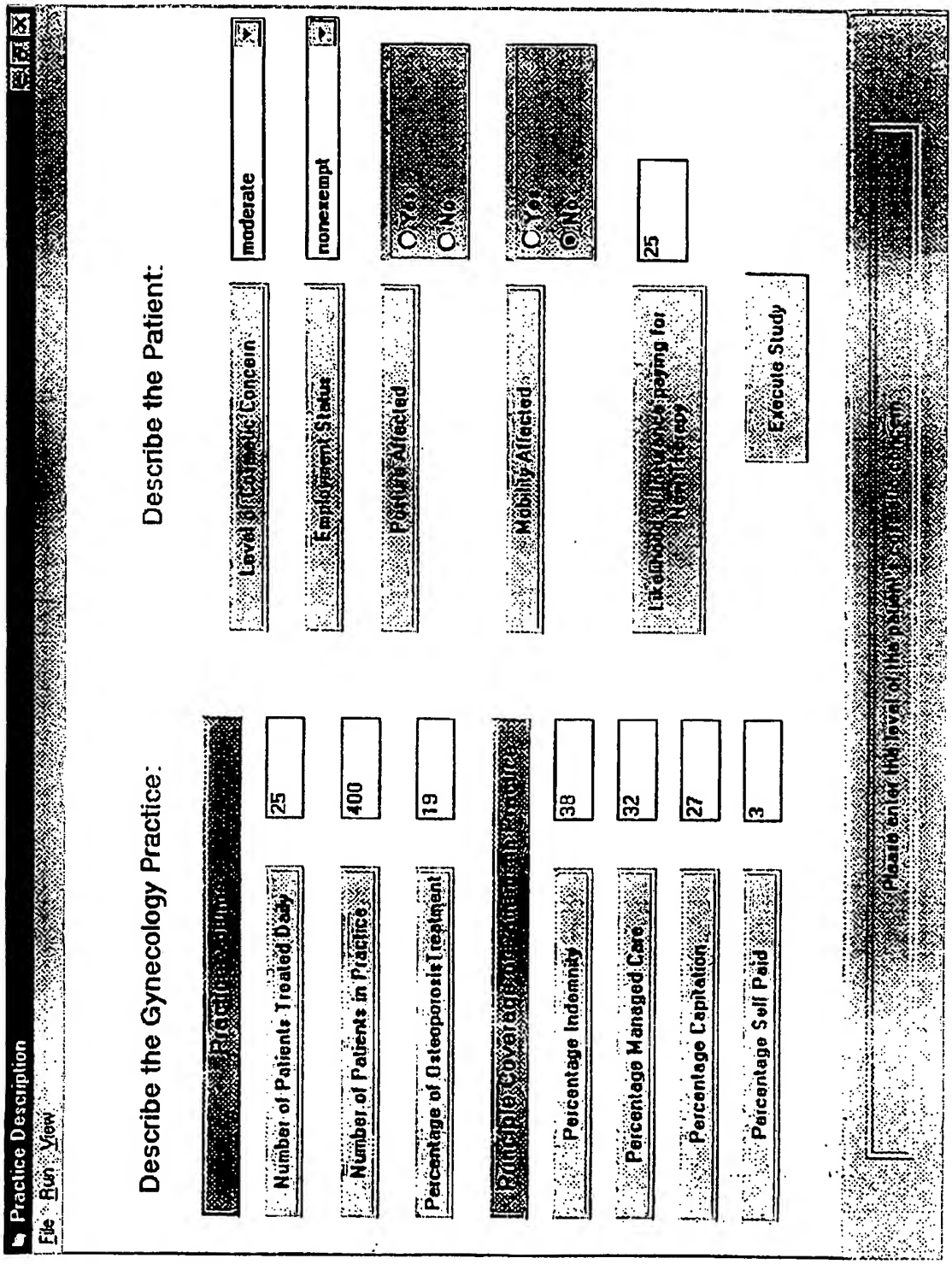
Practice Description
File Run View
Describe the Gynecology Practice:
Describe the Patient:
Number of Patients Treated Daily
25
Number of Patients in Practice
400
Percentage of Osteoporosis Treatment
19
Percentage Indemnity
38
Percentage Managed Care
32
Percentage Capitation
27
Percentage Self Paid
3
moderate
nonexempt
Yes
No
Yes
No
25
Execute Study

FIG. 21

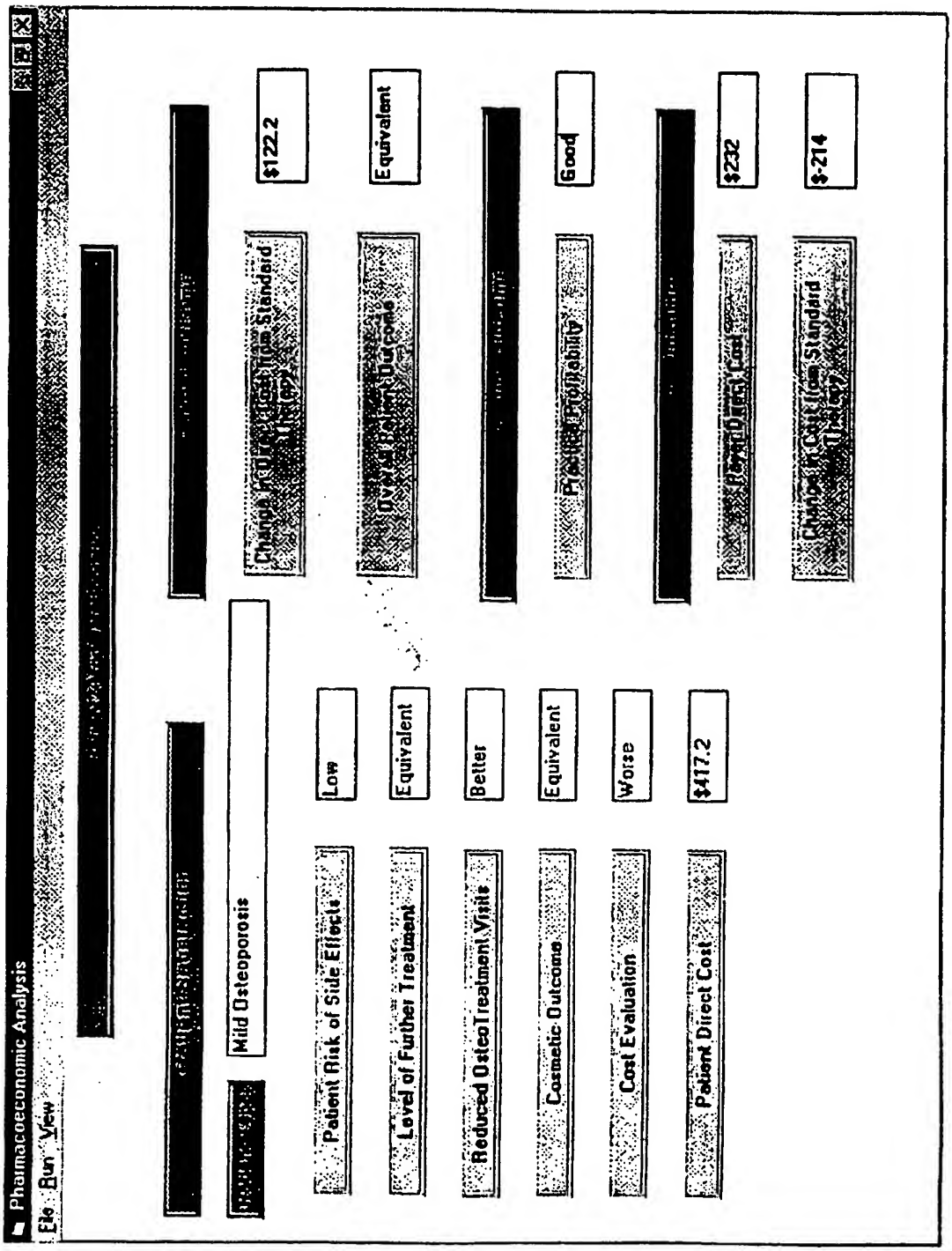
Pharmacoeconomic Analysis
File Run View
Mild Osteoporosis
Patient Risk of Side Effects
Low
Level of Further Treatment
Equivalent
Reduced Osteo Treatment Visits
Better
Cosmetic Outcome
Equivalent
Cost Evaluation
Worse
Patient Direct Cost
$417.2
$122.2
Equivalent
Good
$232
$-214

FIG. 22

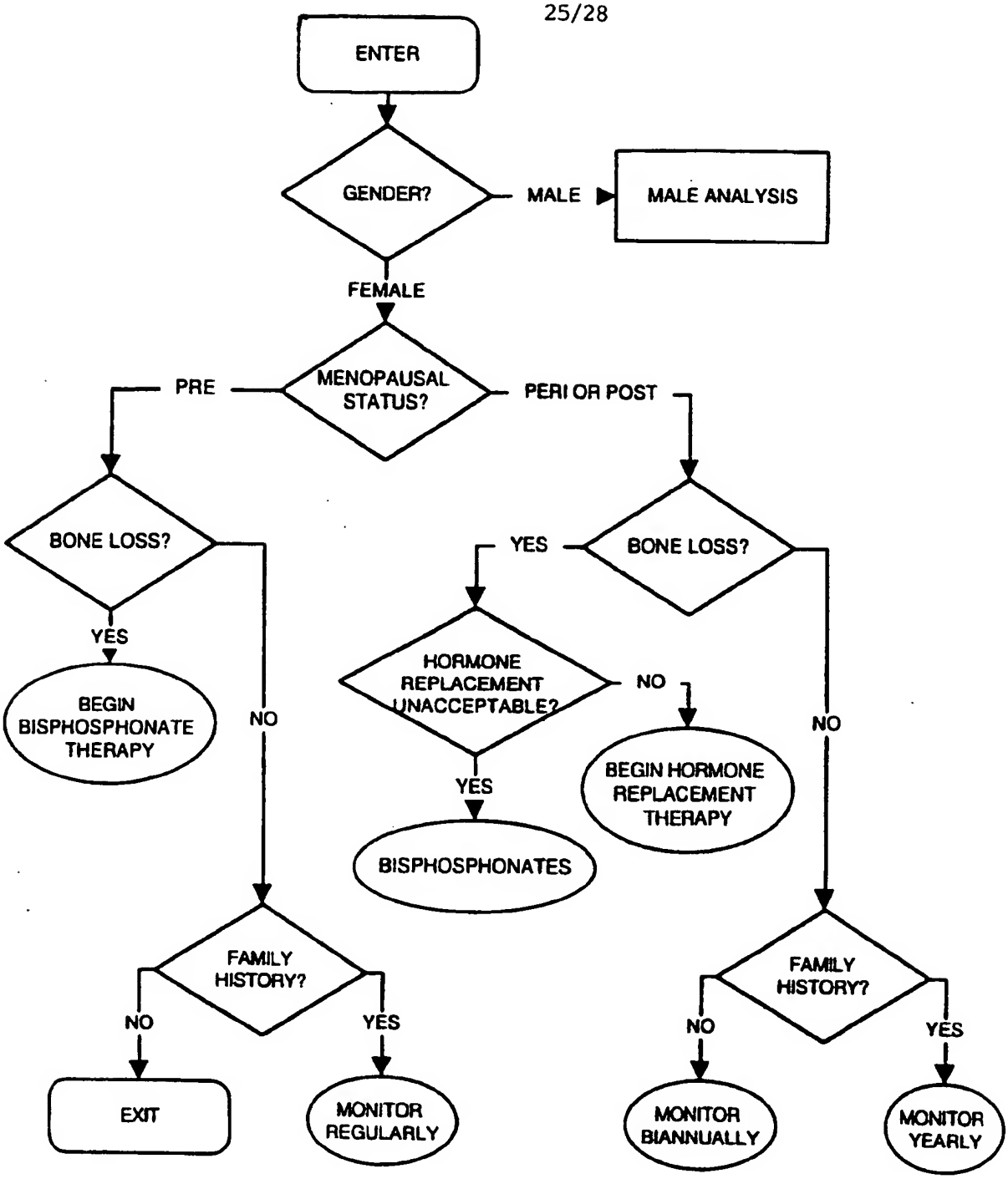
ENTER
GENDER?
MALE
MALE ANALYSIS
FEMALE
MENOPAUSAL STATUS?
PRE
PERI OR POST
BONE LOSS?
YES
BEGIN BISPHOSPHONATE THERAPY
NO
FAMILY HISTORY?
NO
EXIT
YES
MONITOR REGULARLY
YES
BONE LOSS?
HORMONE REPLACEMENT UNACCEPTABLE?
NO
BEGIN HORMONE REPLACEMENT THERAPY
YES
BISPHOSPHONATES
NO
FAMILY HISTORY?
NO
MONITOR BIANNUALLY
YES
MONITOR YEARLY

FIG. 23

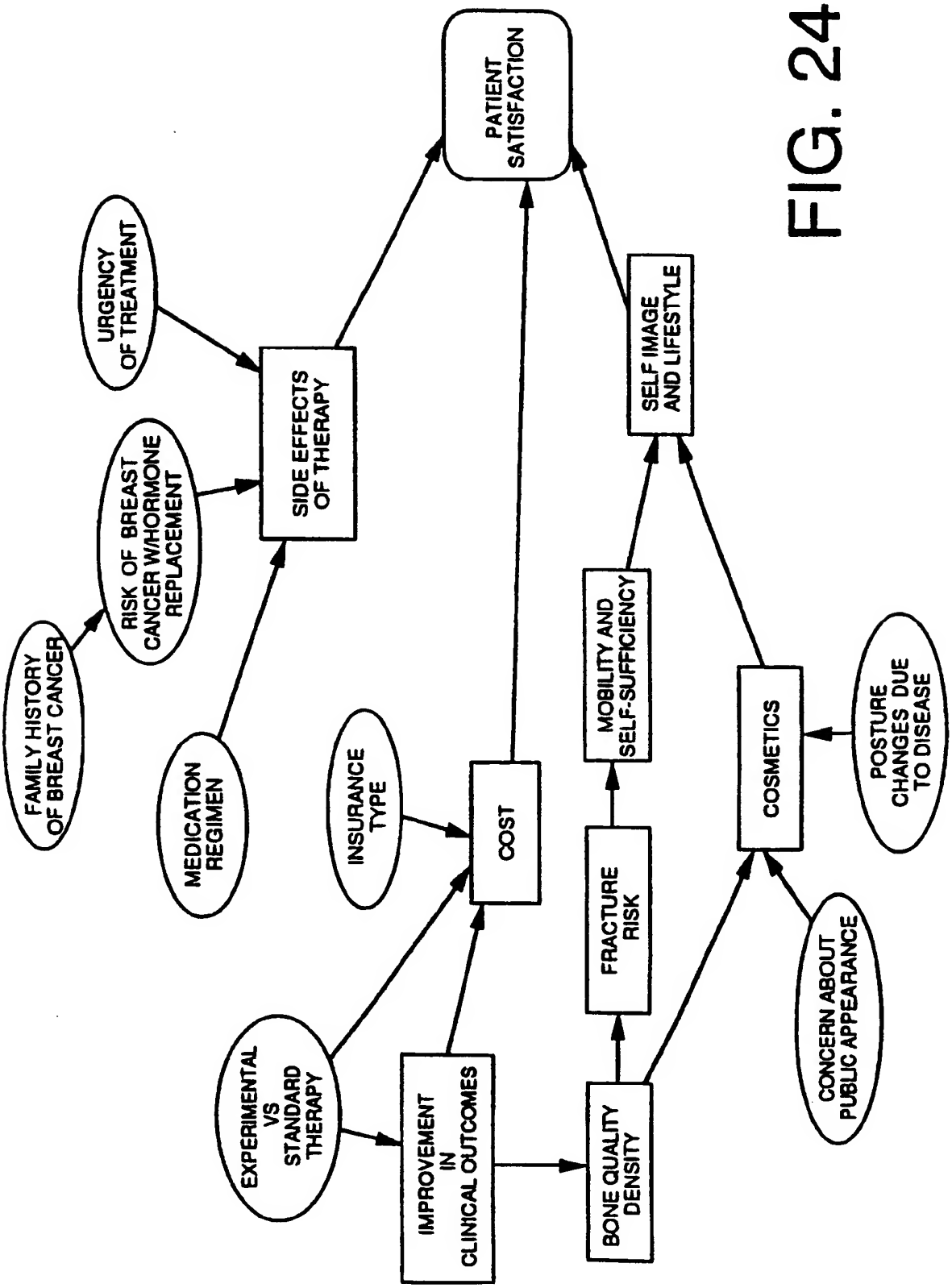
PATIENT SATISFACTION
URGENCY OF TREATMENT
SIDE EFFECTS OF THERAPY
SELF IMAGE AND LIFESTYLE
RISK OF BREAST CANCER W/HORMONE REPLACEMENT
FAMILY HISTORY OF BREAST CANCER
MEDICATION REGIMEN
INSURANCE TYPE
COST
MOBILITY AND SELF-SUFFICIENCY
COSMETICS
POSTURE CHANGES DUE TO DISEASE
FRACTURE RISK
EXPERIMENTAL VS STANDARD THERAPY
IMPROVEMENT IN CLINICAL OUTCOMES
BONE QUALITY DENSITY
CONCERN ABOUT PUBLIC APPEARANCE

FIG. 24

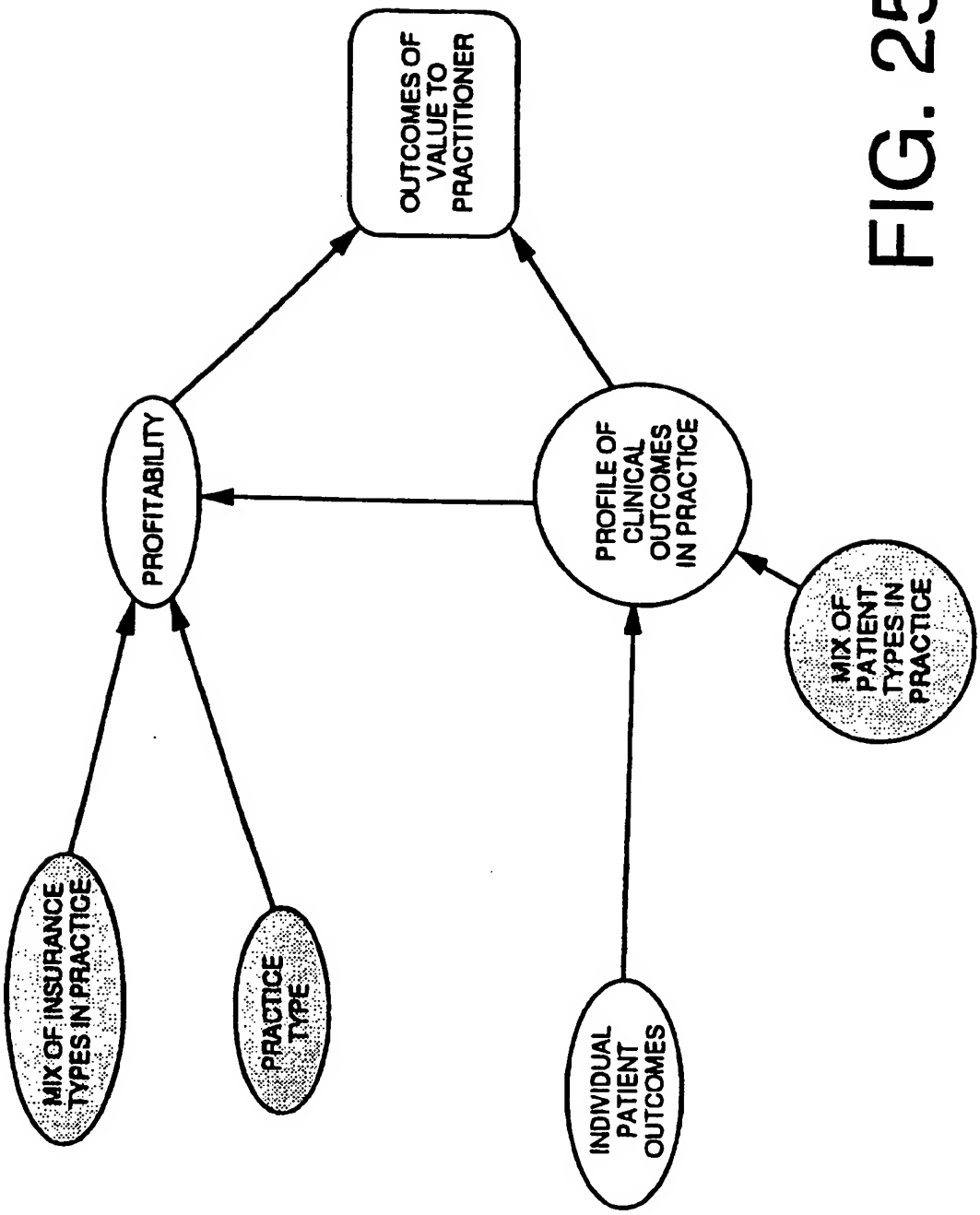
OUTCOMES OF VALUE TO PRACTITIONER
PROFITABILITY
PROFILE OF CLINICAL OUTCOMES IN PRACTICE
MIX OF INSURANCE TYPES IN PRACTICE
PRACTICE TYPE
INDIVIDUAL PATIENT OUTCOMES
MIX OF PATIENT TYPES IN PRACTICE

FIG. 25

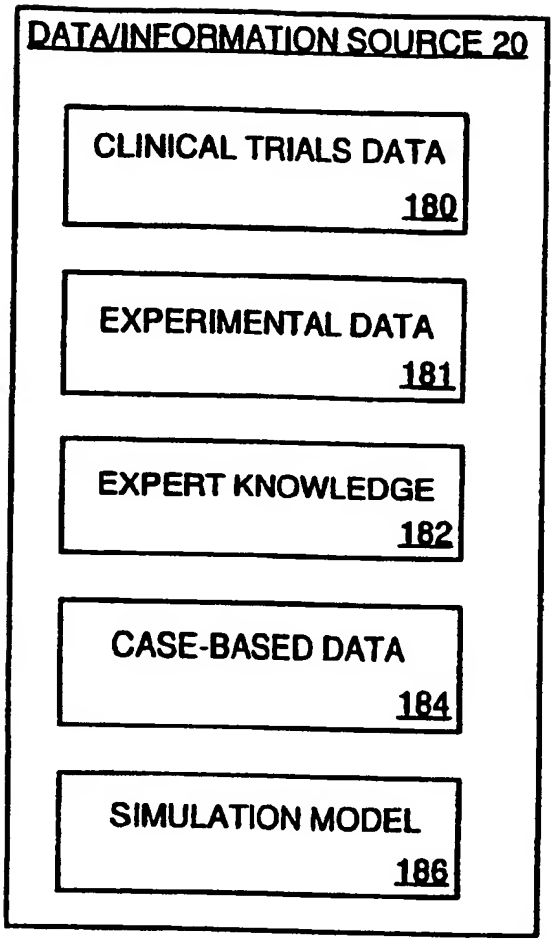
DATA/INFORMATION SOURCE 20
CLINICAL TRIALS DATA
180
EXPERIMENTAL DATA
181
EXPERT KNOWLEDGE
182
CASE-BASED DATA
184
SIMULATION MODEL
186

FIG. 26

INTERNATIONAL SEARCH REPORT

Inten nal Application No
PCT/US 97/08767

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G06F19/00 //G06F159:00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SIEBURG H B: "IN SILICO ENVIRONMENTS AUGMENT CLINICAL TRIALS" IEEE ENGINEERING IN MEDICINE AND BIOLOGY MAGAZINE, vol. 15, no. 2, 1 March 1996, pages 47-59, XP000558491 see the whole document ---	1-61
X	MORGAN ET AL: "the cybermensch simulation server for the planning of clinical trials" INTERACIVE TECHNOLOGY AND THE NEW PARADIGM FOR HEALTHCARE, 1995, pages 445-454, XP002040954 see the whole document ---	1-61

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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2

Date of the actual completion of the international search	Date of mailing of the international search report
17 September 1997	24.09.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Guingale, A

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INTERNATIONAL SEARCH REPORT

Inter. nal Application No
PCT/US 97/08767

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SIEBURG: "methods in the virtual wetlab I : rule-based reasoning driven by nearest-neighbor lattice dynamics" ARTIFICIAL INTELLIGENCE IN MEDICINE , vol. 6, 1994, pages 301-319, XP002040955 see the whole document	1-61
A	WO 92 04860 A (MEDSIM INC) 2 April 1992 see page 7, line 13 - page 8, line 13	1-61
A	WO 94 00817 A (HEALTH RISK MANAGEMENT INC) 6 January 1994 see page 2, line 26 - page 3, line 21	16,51
P,X	WO 96 32684 A (MEDICAL SCIENCE SYSTEMS INC ;KORNMAN KENNETH S (US); FINK PAMELA K) 17 October 1996 see the whole document	1-61

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter nal Application No
PCT/US 97/08767

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9204860 A	02-04-92	AU 8391091 A	15-04-92
WO 9400817 A	06-01-94	AU 673369 B	07-11-96
		AU 4652293 A	24-01-94
		AU 679889 B	10-07-97
		AU 6550096 A	31-10-96
		CA 2121245 A	06-01-94
		EP 0600081 A	08-06-94
		NZ 254452 A	26-04-96
		US 5583758 A	10-12-96
WO 9632684 A	17-10-96	US 5657255 A	12-08-97
		AU 5484596 A	30-10-96

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